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Vol. 189, No. 4769 SATURDAY, MARCH 25, 1961 2s. 6d.

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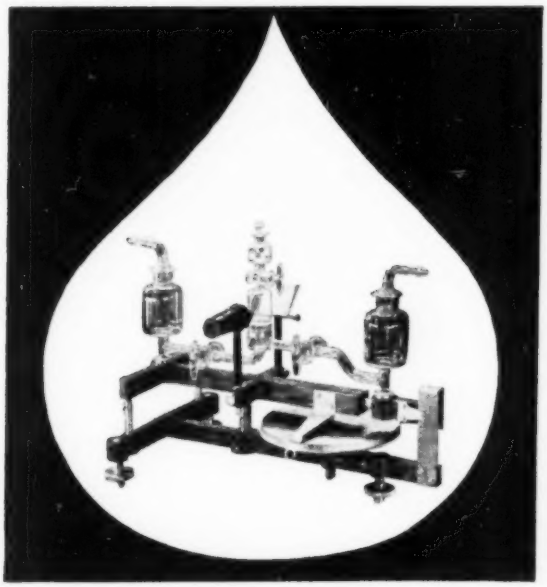

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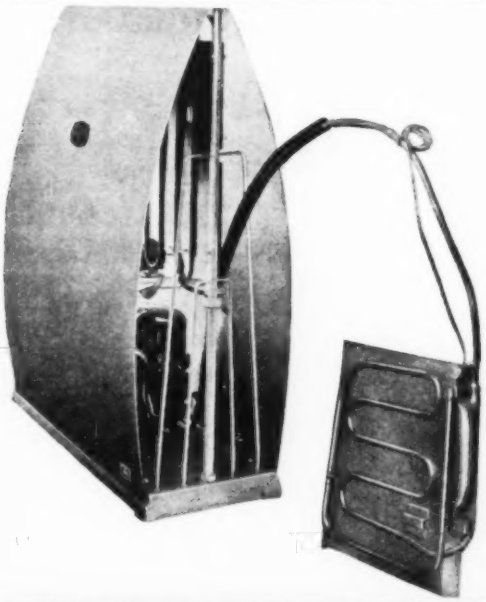

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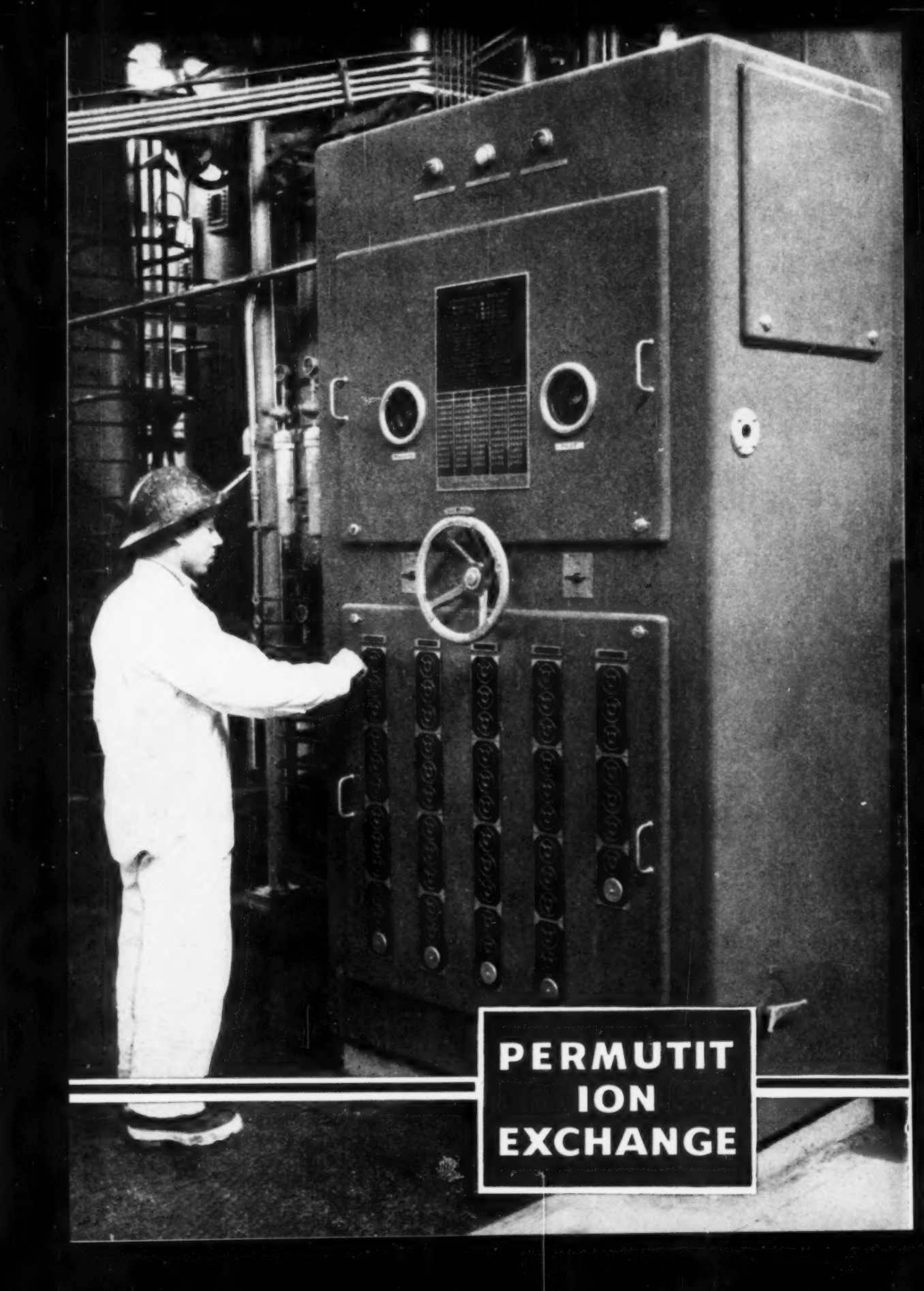
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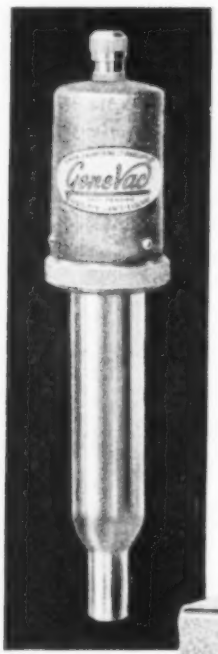

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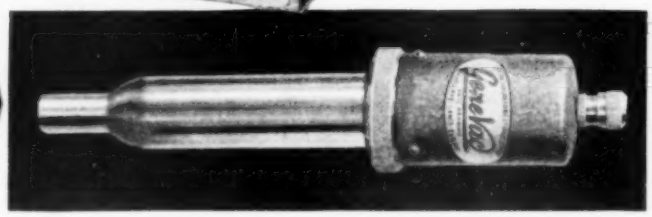

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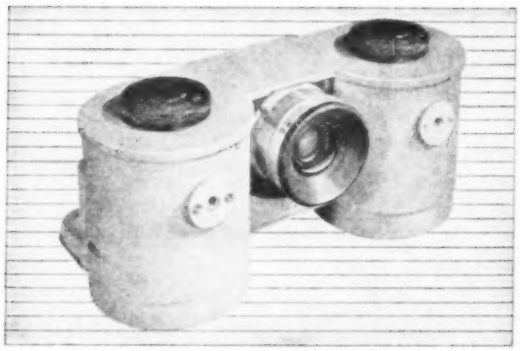

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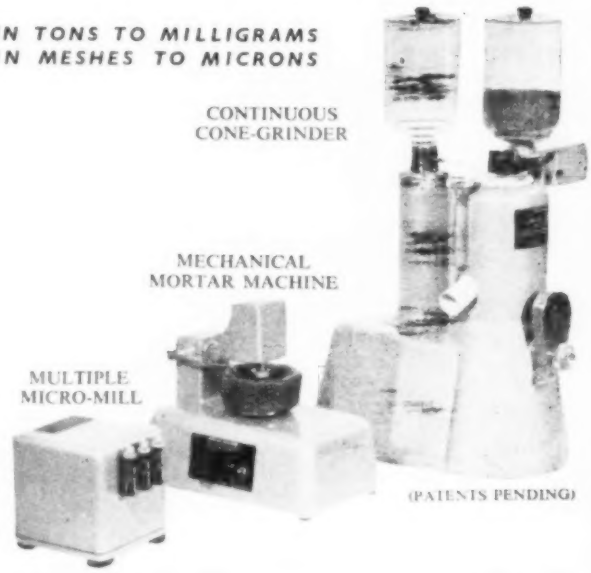

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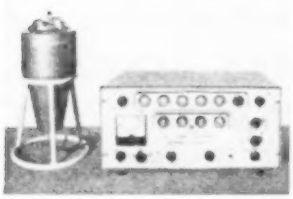

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THE UNDER-DEVELOPED TERRITORIES OF THE WORLD

IT is not surprising that in the debate in the House of Lords on January 25 on the North Atlantic Treaty Organization reference should be made to the recent report, *Increasing the Effectiveness of Western Science* (see *Nature*, 188, 879; 1960), and particularly to the proposal to create an Atlantic Institute of Science and Technology, a proposal which was strongly supported by Earl Jellicoe. Although Lord Carrington, who replied on the debate for the Government, agreed that the proposal merited serious consideration, he declined to commit the Government until the working group, on which Sir John Cockcroft is the United Kingdom member, had reported. While, however, there was other support in the debate, particularly from Lord Gladwyn, the Baroness Elliot and the Earl of Listowel, for the work which the newly formed Organization of Economic Co-ordination and Development of the North Atlantic Treaty Organization could do in co-ordinating all scientific activity, including the encouragement of the production of scientists and technologists, a notable, if not surprising, feature of the debate was the way in which those activities were related to the task of helping the under-developed territories.

This was seen as a moral responsibility, an important aspect of economic policy, and an essential element in the effective defence of the Atlantic Community. The Earl of Listowel, for example, welcomed the establishment of this new Organization as bringing Canada and the United States for the first time into full economic co-operation with other countries of the NATO group in Western Europe. This would facilitate the prior consultation and co-ordination of trade and economic policies that are essential if the West is to do more for the development of the under-developed countries, which still receive most of their capital investment and technical skill from the West. Lord Ogmore, in opening the debate, had stressed the need to increase assistance to the under-developed countries, and it was a key *motif* of the debate that technical assistance is an essential aspect of Western defence policy and in countering the social and economic challenge of Communism in those countries.

It is remarkable, therefore, that this theme should be absent when the Overseas Service Bill received its second reading in the House of Commons on January 24. The Bill was generally welcomed in the debate, and in moving the second reading the Colonial Secretary, Mr. Iain Macleod, stressed that when the Bill became law there would be a three-point structure in the Service, one of which was a vast scheme of technical assistance; nevertheless, the debate generally was concerned rather with the other two points—the schemes of compensation and the public officers' agreement. Mr. Macleod could not add anything to his announcement in December that the Government is studying the establishment of a department or a ministry of technical aid or assistance, except that he hoped the results of this study would be available in a few weeks; though he remarked that he regarded the Bill, which put heavy expenditure on the British taxpayer, as the most important proposal in relation to technical aid for the under-developed countries of the Commonwealth to be put before the House since the Colonial Development and Welfare Act.

Mr. Marquand, for the Opposition, agreed that the Bill contains far-reaching proposals, potentially of great value to the emerging countries, especially within the next five or ten crucial years of their development, and he thought that the implementation of its provisions would contribute to a world-wide extension of technical assistance and expert aid in the provision of the essential structure of development—the improvement of education, public health, agriculture, etc. Mr. P. Wall expressed the hope that Britain would go further than the Ministry for Overseas Aid which Mr. Macleod is at present considering, and endeavour to lay a foundation for the creation of an Overseas Service with interchangeable posting, to serve foreign countries as well as Commonwealth countries and provide administrators and technologists for United Nations organizations and for technical aid throughout the world. He believes there is a great future in this idea, and that development along such lines would ensure that the British genius for administration is not lost to the world.

Dr. Barnett Stross strongly supported the same idea, and, while concerned primarily with medical aid, suggested the creation of a Commonwealth Advisory Council to advise the Minister on medical and technical assistance generally. These suggestions received no comment from Mr. H. Fraser, the Under-Secretary of State for the Colonies, in replying on the debate. Although the debate was indeed concerned largely with the way in which the provisions of the Bill would affect existing officers of the Service, the importance of the contribution which Britain is making to technical assistance was fully recognized, and even the magnitude of the financial obligations which Britain will assume under the Bill was unchallenged except by Sir Kenneth Pickthorn. Mr. Macleod estimated the financial cost at possibly £150 million during the next ten years, and when to this are added the contributions under the Colonial Development and Welfare Acts of more than £25·5 million a year and of bilateral and multilateral assistance of roughly £140 million a year in 1959–60, the magnitude of Britain's effort will be appreciated.

The financial contribution, however, is only one aspect. The demand made on the scientific and technical resources of Britain, particularly in manpower, has also to be considered, and it is in this respect that the last report on *Colonial Research* was so disappointing. The Council for Scientific and Industrial Research, the Nature Conservancy and the Agricultural Research Council, in addition to the

Overseas Research Council, make important contributions to research overseas in various fields; but there was no evidence in that report that the Overseas Research Council is attempting to provide a conspectus of the overall effort and the resources available. All the research councils are responsible to the Minister for Science, but the report provided no evidence that the Overseas Research Council is, in fact, doing anything that the Advisory Council on Scientific Policy could not do, or even to justify the change of name from the Colonial Research Council.

Difficult as they may be, the questions of co-ordination of effort and of communication are increasingly important, and it is as well to note that last year the Overseas Development Institute was formed to serve as a centre to which all those interested in the problems of developing countries could turn for information about the needs of those countries, and the action that is being taken to meet them. The Institute is intended to become a central office of information of this field generally, and also to serve as a centre in which those interested in particular aspects of these problems can meet and exchange views. Besides helping to make people dealing with such problems in government, academic, industrial or commercial undertakings aware of each other's activities, and to bring together those in the United Kingdom who are concerned with these problems and those who, in the developing countries themselves, have intimate knowledge of them, the Institute is intended to keep the public informed of what is going on in this field, of the needs of the developing countries and of what the industrialized countries can and should do to help.

The Institute is being financed by the Ford Foundation and by contributions from industrial and commercial undertakings in the United Kingdom, and it clearly envisages a wider field than the Overseas Research Council or even the Advisory Council on Scientific Policy could be expected to cover. Nevertheless, its formation points to a matter to which the Minister for Science might well give some attention and which should not be overlooked in the study now being made of the most appropriate means of channelling technical aid. The scale on which Great Britain is now contributing, financially and in trained man-power, to overseas development and welfare in the technical and scientific fields makes it imperative that that effort should be effectively co-ordinated and related realistically to the resources of the country, and to its other commitments and demands, as well as to the needs of the under-developed territories.

Particular reference was made to the Overseas Development Institute by Prof. P. M. S. Blackett in his Hinchley Memorial Lecture to the Institution of Chemical Engineers on February 15. Discussing "Science and Technology and the Developing Countries", he returned to a main theme of his presidential address to the British Association just over three years ago, and particularly to aspects of the general problem which were the subject of the symposium on "World Food and Population" in the Association's meeting at Cardiff last September, on which indeed Prof. Blackett drew considerably. It is essential, he said, in the first place, that a young and poor country, setting out on the difficult road of rapid social, economic and technological development, should have a clear idea of what are the right priorities for its investments; and, like Lord Fleck at Cardiff, he pointed out that the under-developed countries must concentrate on a higher yield per acre, rather than, as in Western agriculture, on greater output per man. Until there is plenty of alternative employment in the factories, the saving of agricultural labour creates more problems than it solves; in most parts of Asia the problem is really to devise new technologies which make man-power more efficient without much capital expenditure.

Since the improvement of agricultural yields is the most vital single step in much of South-East Asia, and in particular in India, and because the chemical engineer produces the plant required for the manufacture of the essential fertilizers, pesticides and selective weed-killers, Prof. Blackett considered this aspect of agriculture in the under-developed countries in some detail. The problem is fundamentally that of the application of known methods of production of chemical aids to agriculture and their use; this involves much in the way of large-scale field-trials and experimental farms. Prof. Blackett also suggested that the resources of modern technology could be used to design plant, such as that for the fixation of nitrogen, which is economically more suitable for an under-developed country short of capital but with abundant labour. Detailed technological–economic studies of the possibilities of plants of various sizes ranging down to a small plant with the lowest possible capital cost might be very rewarding; and if any could be brought below £70 per ton a year they might be of great value. The rate of growth of Indian fertilizer production is primarily limited not by lack of scientific knowledge or labour, but by lack of capital.

There is a further factor to consider. While the cost of the optimum size of plant is in the region of £30 million, in general, central governments alone can sponsor them. If, however, the cost could be reduced to £1 million or less, in some circumstances they might come within the scope of State or local governments, or even of private native enterprise; this would be in line with the tendency for increasing stress to be placed on the development of moderate-scale industry right down to the village level. Further, the rapid spreading of technology in this way throughout a country has an important bearing on technical education, and Prof. Blackett suggested that the training given to the operatives could make a vital contribution towards raising the level of technical education.

Putting his theme into more general terms, Prof. Blackett advocated much more study by Western industrialists of the requirements of the developing countries for all kinds of production goods, from large- and small-scale plants to simple tools, taking

account both of the latest technical developments and of the specific economic and social conditions of these countries. Further, he suggested that Western firms operating in under-developed countries should deliberately plan their educational or training facilities in excess of their own needs as a considered contribution to the general technical education of the country in which a particular firm is operating. This he intends should apply to the training of native personnel both in their own country and in the United Kingdom; and from the trend of Mr. Anthony Tuke's remarks, in his chairman's address at the recent annual general meeting of Barclays Bank, on the needs of under-developed countries and the importance of contributing the investment which they require, it would seem that some such response may increasingly be expected.

There is, moreover, strong support to be found for Prof. Blackett's views in the presidential address which Prof. Abdus Salam delivered to the Pakistan Science Congress at Dacca on January 11. Prof. Salam, who referred to Prof. Blackett's address at Dublin in 1957, began by suggesting that acquisition of the requisite technological skills and investment of at least 5 per cent of the national income in the appropriate productive enterprises are the major pre-requisites of self-reinforcing growth. Japanese experience, he said, has demonstrated that the necessary technology is easy to acquire; Russian experience that priorities on heavy industry accelerate the growth, and Chinese experience that labour is itself a form of capital. So far as Pakistan is concerned, Prof. Salam urged that a political group determined to eradicate poverty is a third pre-requisite, and he thought that the new five-year plan reflects the emergence of such a group. The plan recognized the need for bold planning for agricultural development, for exploiting minerals and for heavy industry, and also that liberal provision for developing technological and scientific skills is the wisest investment a nation can make.

The plan aims at a 10–15 per cent capital investment, of which 3–4 per cent is required in foreign exchange and must come from the advanced countries in the form of long-term loans or gifts, and Prof. Salam readily acknowledged that this has involved real sacrifice on the part of those countries. The plan envisages the establishment of heavy industry, particularly steel, with an output of 400,000 tons, and the manufacture in place of import of fertilizers. The major effort, however, is in the provision of the necessary technical skills, including provision for an output of 7,000 technicians a year. Prof. Salam believes that 1961 may mark the beginning of a new era in Pakistan in respect of scientific research and training programmes. He recognized that the success of the Plan depends on some factors beyond Pakistan's own control, but Pakistan's scientists, he said, can none the less make an immediate and essential contribution to the elimination of poverty in Pakistan.

Fully as significant, however, as this consensus of opinion as to the needs and possibilities of technical aid, is the extent to which the whole problem is now being discussed objectively. Mr. A. Schonfield's lucid and comprehensive analysis, accompanied by some provocative suggestions, in his book, *The Attack on World Poverty*, published last year, dealt indeed with one particular aspect and stressed primarily the part that the United Nations should play. Although support for his views may have been somewhat shaken by subsequent developments in the Congo, his arguments as to the need for some re-organization, and in fact for effective co-ordination of the work of the numerous agencies, in spite of the difficulties involved, have been strengthened independently of the soundness of Mr. Schonfield's particular suggestions.

Perhaps even more significant, however, is the discussion of this problem in an article, "The Hungry Two-thirds", which appeared in the *Westminster Bank Review* of November, while earlier in the year the American Academy of Political and Social Sciences devoted the May issue of its *Annals* to a symposium of papers dealing with "International Co-operation for Social Welfare—A New Reality", a feature of which was the stress laid on the need for such technical assistance to be given on altruistic grounds and not in any spirit of competition or as part of a strategy in the defence of the Western world. This point was made again in an article by E. Rabinowitch, "The Atomic Age Doctrine: Common Efforts for Common Aims", which appeared in the *Bulletin of the Atomic Scientists* of September, and the subsequent issue of the same *Bulletin* contained an article by E. S. Prentice, "Significant Issues in Economic Aid for the Developing Countries", which summarized a report of the Stanford Research Institute on that subject. A second article in the same issue (October), by P. T. Bauer, on "Economic Development of Under-developed Countries" was at pains to stress the complexity of the whole problem and the vital importance of the institutional or administrative framework which governments alone can ensure for economic activities.

The need for some sort of master plan to co-ordinate the various types of aid being given to the developing countries, which now runs to something like £1,900 million a year, is one of the points made in the *Westminster Bank Review* article—and the need to diagnose thoroughly the problems peculiar to each country; and it is also recognized that to increase the flow of international aid to the minimum of £1,000 million a year during the next ten years, which P. Hoffmann estimates as required from the West alone over and above the existing level, is not a complete answer. A steadier level of industrial demand for raw materials would of itself enable the developing countries to help themselves more easily. The emphasis in this article is on the political, economic and humanitarian reasons for overseas aid to the developing countries, but it nevertheless lends a good deal of support in general terms to the argument of Prof. Blackett and of Prof. Salam. Incidentally, it also stresses the desirability of channelling such assistance, so far as is possible, through international agencies, and it may be recalled that the World Federation of United

Nations Associations last year renewed its campaign for a ten-year international programme of world economic development.

Ideally, international distribution of technical and other forms of assistance is the right solution; but the objective appraisals of the situation now being made cannot ignore the plain fact that much of the aid distributed in recent years has been wasted, and even without the recent shocks to confidence dealt by events in Africa, the United Nations in its present structure can scarcely be regarded as competent to handle efficiently the flow of development capital and technical assistance on the scale now contemplated. Moreover, in any re-organization, the difficult problems of world government and the sacrifices of national sovereignty involved can scarcely be ignored, nor is it easy to find any recent grounds for supposing that many of the World Powers are prepared to make such sacrifices, however small. Nevertheless, these articles alone show that, at the technical level, the problems are being faced objectively, and President Kennedy's speeches have at least indicated that increasing economic assistance to the less-developed countries will be a central theme of foreign policy under the new American Administration. The United States can scarcely do otherwise than make some effort to ensure that its effort is effectively and efficiently channelled, nor are the voluntary agencies and foundations, like the Rockefeller Foundation, the Ford Foundation and the Carnegie Corporation, to the important contributions of which Dr. L. M. Hoskins directs attention in his contribution to the *Annals of the American Academy of Political and Social Science*, likely to be indifferent to this aspect.

Ultimately, the organization by which overseas aid is distributed, whether technical or financial, must be a matter for determination by governments, and that applies alike to the United Nations and elsewhere. It is not an easy problem to solve, nor is clear and constructive thinking the only condition of success. Widespread public understanding of the issues and the reasons for the sacrifices involved is no less imperative, and for that reason alone, the objective discussion of overseas aid in all its aspects cannot be too wide-spread. With special aspects scientists and technologists have their own particular and direct concern—Dr. E. F. Witto discussed the development of professional leadership in his contribution to the American Academy's symposium—and it is important that they should see that all the implications of such demands on the limited scientific and technical resources and man-power of Britain are fully and clearly understood; the general problem is one to which as citizens they can scarcely be indifferent. While their first concern may well be with the scientific and technical aspects, they have no less the opportunity and responsibility to see that the whole problem is objectively discussed, and to ensure that all the implications of aid on the scale now required, more especially in respect of international organization and administration, are fairly faced and resolutely and honestly handled.

CLASSICAL PHYSICS AND MODERN TECHNOLOGY

Physical Methods of Organic Chemistry

Part 1. Edited by Arnold Weissberger. (Technique of Organic Chemistry, Vol. 1, Part 1.) Third completely revised and augmented edition. Pp. xii + 918.

Part 2. Edited by Arnold Weissberger. (Technique of Organic Chemistry, Vol. 1, Part 2.) Third completely revised and augmented edition. Pp. xii + 895–1797 + 21.

(New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959, 1960.) 184*s*. each.

IT was said, some forty years ago, of a prominent teacher of the then rapidly expanding subject of physical chemistry that he would attract to his laboratory many enthusiastic students by the epigram: "What you have called physics we here call chemistry". The forefronts of research in physics and chemistry have, since then, diverged, but it is evident to-day that twentieth-century chemistry has engulfed nineteenth century physics, for chemists and chemical technologists now make extensive use of exact measurements of the physical properties of different forms of matter.

With the widening of the scope of chemical science and the rapidity of the advancement of organic chemistry towards the biological sciences and the technologies of medicine, it is becoming more and more difficult for any chemist to have an adequate grasp of the principles underlying many types of physical measurements that he may wish to carry out, or of potentialities of available apparatus. It is therefore necessary for one to be able to find easily, on library shelves, authoritative treatises that review, in an up-to-date manner, the technological potential of both classical and modern physics. Since 1946 the series of reference volumes, edited by Arnold Weissberger and issued by Interscience Publishers under the general title *Techniques of Organic Chemistry*, has been recognized as a comprehensive, reliable, publication of this character, though why these books should, by title, be directed more specifically to organic than to inorganic chemists appears to be but a fad of the publishers.

Books of reference must be kept up to date, and now Vol. 1 of the series, that is, *Physical Methods of Organic Chemistry*, has been divided into four parts. Two of these parts have appeared so far in 900-page volumes costing more than £9 each. The periodic reprinting and modernizing of a standard reference work is essential, but in this case the wisdom of the American motto 'bigger and better' can be questioned, for a number of the chapters of these new volumes strike me as being obsolescent in that they deal with measurements of types that few chemists and fewer physicists would deem worth conducting to-day. Still, the book has been revised thoroughly throughout.

Part 1 contains new, short, chapters on automatic control, automatic recording, weighing (mainly a summary of formal theory) and determination of particle size and weight. These are of importance to technologists who need to service complex instruments. Older chapters, often expanded, deal with

temperature measurement, calorimetry, determinations of melting and boiling points, of vapour pressure, solubility, viscosity, surface tension, osmotic pressure and with work on mono-layers. Part 2 contains one new chapter. This deals with X-ray microscopy, which, as the writer admits, has not yet much applicability to chemistry. The others deal with diffusivity, the use of the ultracentrifuge, with refractometry, with crystal measurement, with microscopy (in great detail), with X-ray crystallography (far too briefly) and with both electron and neutron diffraction. Few of these have been changed significantly in this edition, and indeed there is little of new import to be said about several of these techniques. However, it is rational to survey established experimental methods before dealing with others of more recent origin. Furthermore it is to be hoped that the forthcoming Parts 3 and 4, which are to deal, *inter alia*, with spectroscopy and both nuclear and paramagnetic resonance, will show that the overall expansion of the treatise is fully justified.

Too much of these first two volumes has evidently been written by physicists for chemists, and a common attitude seems to have been "here is what can be done with this type of measurement; why you should wish to use it is not my concern". So much is the chemical approach missing that I noted quite a few instances in which no mention had been made of novel, yet significant, applications of old techniques, as, for example, uses of calorimetry and of interference refractometry in studying rapid chemical reactions, or of solubility and vapour pressure measurements in determining the purity of optically active compounds.

Many users may find the chapters too theoretical for their liking, but in this respect they would do well to note the dictum of one contributor that "the experimenter should know more of his subject than he needs to apply in attaining the particular accuracy of his present measurements". This caution was rightly followed by notes on the theoretical and experimental limitations of commercial instruments. Such sections throughout the book are well worth reading.

Every specialist who consults this book may find gaps in the treatment of his own topic, but one should be circumspect in not demanding too much of any treatise.

W. A. WATERS

HUMAN GROWTH

Human Growth

Edited by J. M. Tanner. (Symposia of the Society for the Study of Human Biology, Vol. 3.) Pp. vii+120. (London and New York: Pergamon Press, 1960.) 30*s*. net.

THIS, the third volume published on behalf of the Society for the Study of Human Biology, is a record of the proceedings of one of the symposia which the Society convenes periodically (see *Nature*, **186**, 19; 1960). The topics are many and varied and range from age-changes in primates and their modification in man, contributed by Prof. Adolph Schultz of the University of Zurich, to the effects of race and climate on human growth as exemplified by studies on African children. The latter studies were initiated by D. F. Roberts, University of Oxford, and are of particular significance because the samples were taken not from dwellers in the vicinity of administrative and urban centres, but from remote peoples in tribal and rural areas. They corroborate previous findings showing that African children differ from European children by a tendency towards lower weight for a given height.

Two contributions to the symposium should commend this book to all educationists. The first, by Dr. Roy M. Acheson, examines the effects of nutrition and disease on human growth, and brings ample experimental evidence to show that even a very brief insult can greatly retard the growth of a child. The other, by Dr. D. W. Boyne, is concerned with secular changes in the stature of adults and the growth of children, especially relating to changes in the intelligence of 11-year olds. Besides confirming that the intelligence of boys and girls varies with respect to one another at different ages, the author produces additional evidence to confirm that the intelligence of girls over the age of eleven has been improving relative to that of boys since before 1939. Whether this is due to real change in the innate intelligence or to change in the nature of the tests is not known. It is certain, however, that great progress in our knowledge of human growth has been made since Sir D'Arcy Thompson concerned himself with biological gradients and that, besides educationists, this book has much to interest anatomists, zoologists, anthropologists and medical practitioners.

DECISIONS, VALUES AND GROUPS

Decisions, Values and Groups

Vol. 1: Reports from the First Interdisciplinary Conference in the Behavioral Science Division, held at the University of New Mexico. Edited by Dorothy Willner. (Sponsored by the Air Force Office of Scientific Research.) Pp. xxix+348. (London and New York: Pergamon Press, 1960.) 80*s*. net.

THE foreword of this book is by Dr. Charles E. Hutchinson, chief of the Behavioral Science Division of the Air Force Office of Scientific Research in Washington; the introduction is by Dr. Anatol Rapoport; and the preface is by the editor. It is divided into five parts: (1) Mathematical Models in Decision Processes; (2) Conceptualizations and Designs for Research in Values; (3) Theoretical Contributions to Small Group Research; (4) Psychodynamic Patterns of Behaviour; (5) Special Military Problems.

There are twenty-three independent papers, too many even to list. Only one paper necessitates an acquaintance with higher mathematics. It is entitled "Stochastic Choice and Subjective Probability". But the experiment conducted would be regarded as somewhat simple by a student of Prof. M. S. Bartlett's *Stochastic Processes*.

The significant characteristics of the book seem to be that decision processes and evaluative processes are regarded as essential scientific concepts. That is, no science can proceed without a system of values. But here lie the most difficult problems of human endeavour and "no quick-fixes or break-throughs" are claimed. Perhaps progress will be reported in Vol. 2.

The method of attack was to select a large team of highly qualified younger scientists from various behavioural sciences. Each was assigned a problem and they all attended an eight-week work-session during June 17–August 10, 1957, for interdisciplinary activity, that is, a kind of prolonged super-symposium. Such a method clearly has advantages, but there is the view that new ideas are produced by individuals and not by committees, the young research worker receiving daily inspiration and guidance in the laboratory of his chief. Both methods may be combined.

Dr. Rapoport writes: "The title of this volume reflects a delineation of areas of study which is different from the traditional delineations suggested by university departments. There is no university department concerned with either 'decisions', 'values', or 'groups'. Decisions are studied, of course, by psychologists, by political scientists, and by military strategists. A 'decision theory', however, should transcend these special content areas". Similarly, "Values are studied by philosophers, by economists, by psychiatrists and by anthropologists from different points of view and by different methods".

The change of pattern in air-force research during the past forty-five years is obvious. In the First World War it was largely sensory. Many of the problems were solved under the direction of two men working in close collaboration, the physiologist, General Wilmer of the United States, and the psychologist, Prof. Spearman of Britain. Thus, when more than seventy ace pilots were tested by means of a battery of ocular tests, it was found that most tended to do well. One exception, who did badly in one test, was a famous ace who lacked the ability to land his plane undamaged. He was always given another. In the Second World War, air force research was more concerned with intellectual capacities. At the present time, we have noted that research has embarked on the scientific study of values. Is it too sanguine a hope that this will eventually help to abolish war?

LL. Wynn Jones

DISEASES OF ORNAMENTAL PLANTS

Diseases and Pests of Ornamental Plants

By Pascal P. Pirone, Bernard O. Dodge and Harold W. Rickett. Third edition. (An official publication of the New York Botanical Garden.) Pp. x+775. (New York: The Ronald Press Company, 1960.) 10 dollars.

THIS book follows very closely the plan of the second edition but has been brought up to date by the inclusion of the latest information concerning the control of pests and diseases. In addition, the authors have revised the nomenclature of the pathogens to accord with the present views of taxonomists and plant pathologists. It is also evident from the increased number of entries under the various host plants that many new pests and diseases have been recorded in the United States since the publication of the previous edition twelve years ago.

The book is divided into two parts. The first contains an introductory chapter on "Plant Diseases" in which the diseases are classified and described under symptoms and causes. This is followed by a chapter entitled "Bacteria and Fungi" (viruses are, rather surprisingly, omitted) in which the structure and classification of these organisms are briefly discussed. It is here that one finds (p. 39) the rather sweeping statement that "Recent improvements in staining techniques, however, have revealed one to three septa (cross-walls), showing the bacterial body actually consists of two to four cells". Likewise the observation (p. 42) that "The threads (hyphae) of many fungi are composed of fundamental structural units, cells, found generally in plants and animals" is apt to be misleading as it stands. Mycologists will also, no doubt, be surprised to learn (p. 66) that "It should be understood, that every species of fungus now classed among the imperfect fungi will ultimately be found to be connected either with some ascomycete, basidiomycete or phycomycete". The third chapter is devoted to a general account of "Insect and Other Animal Pests" and is followed by one on "Control". This latter chapter contains much useful information on such topics as disinfection of seeds, bulbs, tools, clothing and hands; pasteurization of soil; fungicides, bactericides, insecticides and miticides; spreaders; and equipment. General advice on the choice, preparation and application of fungicides, bactericides and pesticides is also included.

The second part of the book consists of an account of the individual pests and diseases of particular host plants, which are arranged in alphabetical order according to their Latin names. This section appears to cover the subject very thoroughly, although there are omissions such as the failure to mention witches' brooms of *Carpinus* caused by *Taphrina* spp., but such instances are few.

Detailed comparison between the entries of the fungus diseases in this work with those of the second edition shows a number of omissions, but these would appear to be due to the authors having restricted themselves to diseases occurring in the United States. Sometimes, however, the wording in the second edition is such that one is not always clear whether the disease actually occurred in that country. There is one rather odd instance of an entry in the second edition under *Anemone* of rhizome-rot said to be caused by *Sclerotinia tuberosa* for which symptoms are given together with a full account of the fungus. The disease is said to be "irregular in its occurrence. It is found naturally on wild plants, but is not common in gardens around New York City and in cultivated plantings; it can be very destructive", all of which clearly implies its presence in the United States. In the third edition under review there is also an entry of rhizome-rot under the same host, but here the causative agents are said to be *Pellicularia rolfsii* and *Sclerotium delphinii*. No mention is made of a disease caused by *Sclerotinia tuberosa*.

In conclusion, it may be stated that the appearance of this third edition of *Diseases and Pests of Ornamental Plants* will be welcomed by plant pathologists and growers, especially those in the United States, although its usefulness is by no means confined to that country. Its faults are few and relatively unimportant since they are unlikely to cause serious inconvenience to the average person using this volume as a work of reference. It is attractively produced and very well illustrated. Furthermore it is printed in larger type than its predecessor which makes for easier reading.

Derek A. Reid

STREAMING OF INTERSTELLAR HYDROGEN IN THE VICINITY OF THE SUN

By Dr. R. X. McGEE, Dr. J. D. MURRAY and Dr. J. L. PAWSEY, F.R.S.

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OBSERVATIONS of the 21-cm. hydrogen line have provided means for detecting the bulk movement of interstellar gas in our Galaxy. In addition to the well-known rotation about the galactic centre, Oort and Rougoor[1] have recently shown that the gas in the galactic disk, a few kiloparsecs from the centre, displays expansion at velocities of about 100 km./sec. It has been suggested by Kerr[2] that the outward movement may continue, with much reduced velocity, beyond the Sun. If this is so, where does the gas go? Does it stream outwards, above and below the disk? The results to be described here supply evidence for large-scale streaming of the gas in the vicinity of the Sun, but the observed flow does not conform with this simple picture.

The distribution of local neutral hydrogen has been discussed previously by Erickson, Helfer and Tatel[3] and by Davies[4]. We have recently completed a series of 21-cm. observations over the whole sky visible from Sydney with an aerial beam of 2·2° between half-power points and an *H*-line receiver of 48 channels spread at frequency intervals equivalent to 7 km./sec. in radial velocity about the natural line frequency. A full description of this equipment and the analysis of the observations is being prepared for publication.

One of the parameters extracted from the observations is N_H, the number of hydrogen atoms in a line-of-sight column of 1 cm.^{2} section. It is derived from the integrated area of an *H*-line profile. Since the hydrogen is known to be concentrated in a thin layer (only a few hundred parsecs thick), most of the observations, except those near the Milky Way, will refer to gas in the vicinity of the Sun, that is, within a few layer thicknesses. A study of the distribution of N_H in galactic latitude showed it to be consistent with a general stratification parallel to the galactic plane in which a number of large clouds are embedded. These clouds include the Scorpius-Ophiuchus complex subtending some 3,000 square degrees, a large region in Gemini-Taurus-Orion, and its possible extension into Andromeda and Pisces. The examples mentioned are also characterized by *H*-line profiles the half-widths of which are less than 20 km./sec. Such evidence suggests that these local gas clouds are of a compact nature.

An approximate estimate of the neutral hydrogen density near the Sun has been made using: (1) average values of N_H at the different latitudes, and (2) the shape of the distribution in the *z*-direction (that is, perpendicular to the galactic plane) as derived by Schmidt[5]. The density is 0·46 hydrogen atom cm.$^{-3}$, which may be compared with 0·48 hydrogen atom cm.$^{-3}$, obtained by Westerhout[6], for the mean density between circles 8 and 9 kiloparsec. from the galactic centre. It would therefore appear that the Sun is situated in a representative region of the galactic disk.

Another parameter selected for study is the profile peak radial velocity. We have chosen the peak value since a great majority of the local profiles are single peaked and reasonably symmetrical. Thus the peak velocity gives a good representation of the gas velocity and, further, it may be easily and accurately read from the observed profiles. The velocities are referred to the local standard of rest.

The distribution of peak radial velocities is illustrated by the contour diagram of Fig. 1. The 'old' galactic co-ordinate system (Ohlsson) is used and, following convention, l^{I} and b^{I} designate galactic longitude and galactic latitude respectively. This is essentially a schematic diagram based originally on sample data analysis at intervals of 30° and 2° in l^{I} and b^{I}, but afterwards checked at more frequent intervals. The contour interval is 3 km./sec. except for the zero velocity, shown in white, which includes −1, 0, +1 km./sec. values. Positive velocity regions are indicated by light grey and negative velocities by dark grey shading. In the Milky Way region an attempt was made to pick out only the contribution of the local gas, but uncertainties exist here due to possible inclusion of contributions from gas in other spiral arms. Radial velocities exceed 15 km./sec. in magnitude and reach maximum values of ~33 km./sec. in the hatched areas. Velocity values taken from the Leyden profiles[7] and Erickson *et al.*[3] have been used to augment the diagram in the region not visible from Sydney.

The striking feature of the velocity distribution is the extent of the areas of velocities of similar sign and magnitude. Two regions of positive velocity, one centred approximately on $l^{\mathrm{I}} = 10°$ and the other on $l^{\mathrm{I}} = 190°$, extend from the equator to galactic latitudes ±40° over longitude ranges of more than 90° each. Regions of negative velocity lie between these at low latitudes. Negative velocities dominate the picture at high latitudes; the southern cap down to $b^{\mathrm{I}} = -40°$ is almost completely occupied by approaching gas, the northern cap has approaching gas together with a narrow sector near $l^{\mathrm{I}} = 150°$ of diffuse gas of various velocities including those of approach. The prevalence of negative velocities in the polar caps was noted by Erickson *et al.*[3].

The alternating positive and negative velocities in latitudes up to ±30° are clearly associated with differential galactic rotation. It would be of great interest if, in addition, a general gas-flow pattern could be recognized. However, due to the lack of a measure of distance to the observed hydrogen, we cannot assign a particular velocity to be expected in a given direction due to differential galactic

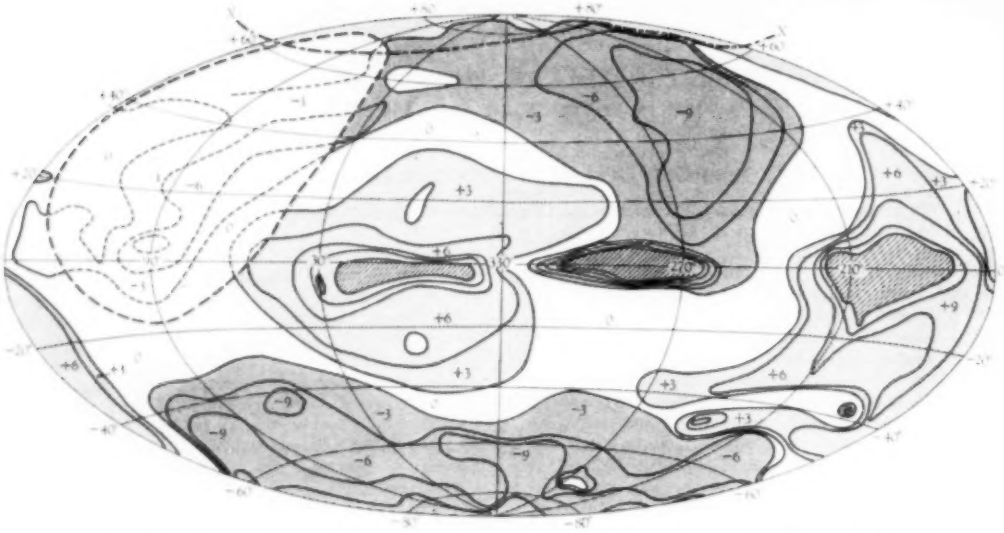

Fig. 1. The distribution of *H*-line peak radial velocities. The contour interval is 3 km./sec. Co-ordinates: 'Old' System, Galactic (Ohlsson). Light grey shading denotes regions of positive velocity, dark grey negative velocities, and white zero velocity (−1, 0, +1 km./sec.). Hatching denotes regions of velocity exceeding 15 km./sec. Diffuse gas of various peak velocities was observed in the region north of +

rotation. But assuming the current rotational model and also that the Sun lies near the central plane of a stratified region of thickness $\leqslant 2z$ we can estimate an upper limit to the radial velocity, v_R, to be expected in a given direction (l^{II}, b^{I}), namely:

$$v_R \leqslant Az \cot b^{I} \sin 2l^{II} \cos b^{I}$$

where A is Oort's constant (= 19·5 km./sec./k.parsec) and l^{II} the galactic longitude in the revised system in which the galactic centre is in the direction $l^{II} = 0$ ($l^{II} \approx l^{I} = 327{\cdot}7$ at low latitudes). z has been taken as 0·11 k.parsec, Schmidt's estimate of the semi-thickness of the hydrogen layer to half density.

Examples of the derived curves are compared with the observed radial velocities in Fig. 2. Two quite definite results emerge. The first follows from the above equation in which the amplitude of the theoretical velocity curve falls to about 1 km./sec. above $|b^{I}| = 45°$. In effect, then, the observed velocities in high latitudes are scarcely influenced by differential galactic rotation and hence local in-streaming of the gas is indicated.

The second result is due to the fact that, no matter how inaccurate the value of z may be, the radial velocity due to differential rotation in circular orbits must pass through zero at the longitudes of the galactic centre and anti-centre (327·7° and 147·7° respectively). The existence of observed positive velocities in these directions, and in directions where the model predicts negative velocities, emphasized in Fig. 2 by the thick segments, means that here the gas has an additional outwards motion. We consider that at low latitudes the other differences between observed and predicted values are within the uncertainty in interpretation.

Referring to Fig. 1 we conclude that at high latitudes, in the range $90° \geqslant |b^{I}| \geqslant 40°$, neutral hydrogen is definitely flowing in from above and below at approximately 6 km./sec. at all longitudes. At low and middle latitudes the gas is flowing away

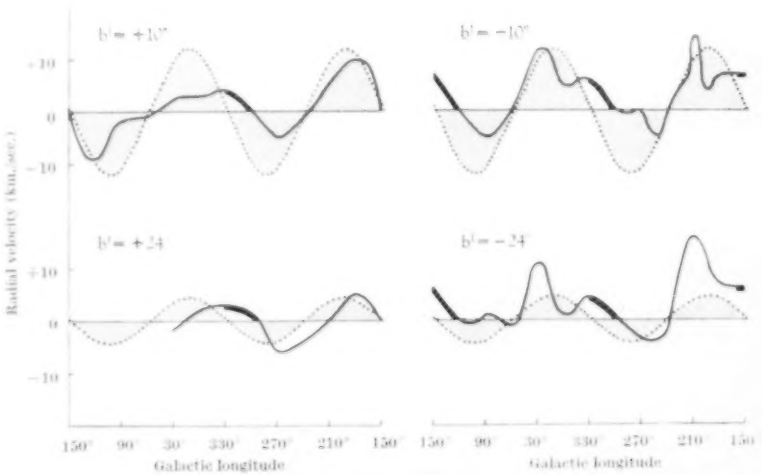

Fig. 2. Examples of curves of radial velocity against galactic longitude. The full curves show observed velocities. The shaded areas give the range of predicted velocities due to differential galactic rotation. The thickened segments of the observational curves indicate definite discrepancies between observation and these predictions

from the Sun in the general directions of the galactic centre and in southern latitudes near the anti-centre at approximately 6 km./sec.

We describe these motions as streaming, but we cannot tell if they are peculiar to our vicinity or whether they form part of a general circulation. Quantitatively, for the polar caps, combination of the velocity of inflow of 6 km./sec. with an estimated density of about 0·5 hydrogen atom cm.$^{-3}$ leads to a rate of inflow of about 10^{-7} $M_\odot$ (solar mass) per square parsec per year. If this flow is general over a substantial part of the galactic disk, the amount of gas flowing in over a ring of 1 k.parsec width at the radius of the Sun would be several solar masses per year, so that the quantities of hydrogen involved would be sufficiently great to make the phenomenon a major feature of galactic dynamics.

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A HYPOTHESIS CONCERNING THE MECHANISM OF GENE ACTION

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Components of a Gene-System

IT is usual to think of the gene as a particle located on the chromosome; but the phenomena associated with the action of a given gene occur in various places throughout the cell and should be considered to comprise a system which I shall designate the gene-system. The gene-system includes at least three separable entities: the receptor, located on the chromosome at the place usually spoken of as the locus of the gene, the transmittor and the effector. This discrimination is based on the fact that the gene is on the chromosome, and the enzyme which the gene controls is almost certainly synthesized in the cytoplasm, since the cytoplasm is the principal site of protein synthesis.

A Gene-System in Saccharomyces

The gene-controlled synthesis of an enzyme, such as melezitase[1,2], in the yeast cell, is initiated by exposure of the cell carrying the gene to various short-chain α-glucosides. In cells carrying the gene controlling the synthesis of melezitase, each of the different α-glucosidic inductors initiates the synthesis at the locus of the gene on the chromosome. The initiatory event results in the production of an enzyme which appears to have the same characteristics irrespective of the inductor. The mechanism which connects the induction at the locus with the final synthesis of enzyme in the cytoplasm is designated the transmittor. Melezitase (which is not present in an unadapted cell)[3] splits many relatively short-chained α-glucosides. It is induced by the five different α-glucosides, namely, turanose (*T*), maltose (*M*), sucrose (*S*), α-methyl-glucoside (*G*) and melezitose (*Z*). The letters *TMSGZ* are used to designate the dominant allele of the gene[3]. Unadapted cells require more than 1 hr. to accumulate detectable amounts of enzyme. The enzyme induced by any one of the inductors acts on all the other inductors and a few other short-chain α-glucosides[2,4] without an induction period, that is, without further adaptation. Because the different inductors seem to initiate the production of the same enzyme, it is inferred that both the transmittor and the effector respond to a stimulus initiated at the receptor, resulting in the production of a single uniform product, irrespective of which one of the five inductors acted as the inducing agent. Any inductor can activate the effector; the effector reacts non-specifically with respect to the specific inductor. These facts led to the hypothesis that the receptor[5], in the nucleus, which responds to a specified variety of inductors, and the effector, in the cytoplasm, which acts uniformly irrespective of which of the specified inductors initiates the action, must be connected by a transmittor.

Anatomy of the Receptor

Some ideas about the anatomy of the receptor have been suggested from the study of a series of multiple alleles which occupy the *TMSGZ* locus. The multiple alleles are distinguished from each other by their different abilities to respond to the five different inductors. Because there are five separable characters, thirty-two different possible multiple alleles might be expected if each character were expressed independently of the other four characters[3]. One allele, *TMSGZ*, responds to any one of the five inductors by the production of enzyme. At the other extreme is the totally recessive allele, designated by five dashes (– – – – –), which does not respond to any of the five inductors. Five other partially recessive alleles of the locus have been discovered: *TMSG* –, *TMS Z*, *TMS* – –, *TM* – – –, *T* – – – –. Cells carrying these alleles respond to the inductors indicated by the capital letters but are incapable of responding to the substances indicated by the dashes. The limitation of the number of alleles proves that the characters are not expressed independently of each other. The fact that only one allele is incapable of responding to turanose as an inductor and that this allele is also incapable of responding to any other inductor indicates that the turanose character is fundamental to the receptor. This suggests that an injury to the locus which renders it incapable of responding to turanose will impair the capacity of the gene-system to respond to any other inductor. The limitation of the number of alleles suggested the hypothesis that the receptor is a conformation composed of at least

five different overlapping patterns each composed of one or more elements[5,6]. Each of the patterns is assumed to fit one of the five inductors and to act as the specific receptor for that particular inductor. The elements of a pattern are assumed to form a template, or a reverse model, or a 'cast', of the inductor. Deformation of any element of a pattern may result in the inability of the particular inductor, for which the pattern is a receptor, to fit the inductor. The various patterns of the total conformation are assumed to overlap in such a manner that the turanose pattern is a component part of each of the other patterns, and it is assumed that injury to an element of the turanose pattern will make it impossible for any of the inductors to fit the conformation. But deformation of an element comprising the melezitose pattern will not prevent the other four inductors from fitting the conformation and bringing forth the production of enzyme.

Mutation by Ultra-violet Rays

Analysis of the mutagenic effects of ultra-violet rays on *TMSGZ* suggests that each pattern has a specifically different sensitivity to ultra-violet rays[3]. When *TMSGZ* is subjected to ultra-violet radiation the different alleles are recovered from among the survivors with approximately the following frequencies: *TMSG* –, 8 per cent; *TMS* ––, 4 per cent; *TM* –––, 2 per cent; *T* ––––, about 2 per cent; and ––––––, less than 1 per cent. If one assumes that *TMSG* – results from injury to the *Z* pattern, the results indicate that the *Z* pattern is more sensitive than any other pattern. Likewise, if one assumes that –––––– is the result of injury to the *T* pattern, the results indicate that the *T* pattern is more resistant than any other pattern. The *M* and *S* patterns are inferred to be about equally sensitive, but more sensitive than the *T* pattern. The *G* pattern is about half as sensitive as the *Z* pattern. The sensitivities of the different patterns may be ranked in the following ascending order: *T*, *M*, *S*, *G*, *Z*.

Gene-Conversion

Multiple alleles are also produced by gene-conversion. The multiple allele, *TMS–Z*, was recovered from cross-breeding experiments presumably as the result of gene-conversion[1]; it was not discovered among the survivors of ultra-violet irradiation. This suggests that the mutation of *TMSGZ* to *TMS-Z* (which involves injury to the *G* pattern without injury to the *Z* pattern) may occur in a heterozygote but is not commonly produced by ultra-violet radiation. A complete series of alleles indistinguishable from those produced by ultra-violet irradiation was recovered by tetrad analysis of heterozygotes. It was inferred that this series of alleles had been produced by gene-conversion[7].

X-ray Mutations

A third procedure for producing the different multiple alleles is X-irradiation. In contrast to ultra-violet - induced mutation, treatment with X-rays has produced only two types of mutants from the *TMSGZ* dominant allele; namely, *TM* ––– and ––––[4]. Although ultra-violet rays may destroy one pattern without affecting contingent patterns, the results suggest that the effect of X-rays may be 'spread' over several contingent patterns. For example, the *TM* ––– mutant might result from a 'hit' in either the *G* or the *Z* pattern which spreads to include the *S* pattern. The –––––– mutant (which is characterized by damage to the *T* pattern) might be the result of a 'hit' which spreads to the *T* pattern from as far 'away' as the *S* pattern. Many lethal mutants were probably produced by X-rays but were not recovered. The mutants which survived and were recovered might have been produced by impacts of low energy. These inferences are consistent with the generally held view that ultra-violet rays are much less devastating in their mutagenic action than the X-rays.

Gene-Transformation by Substrate

Gene-transformation is defined as controlled mutation produced by a chemical reagent. In the preceding experiments, mutations from normal to defective were described[3]. Several reports from this Laboratory have concerned controlled reverse mutation from defective to normal by exposure of cells to specific carbohydrates[8,9]. Exposure of different partially recessive members of the *TMSGZ* series of multiple alleles to various specific substrates (especially to melezitose) has effected reverse mutations from various partial recessives (*TMSG* –, *TMS* ––, *TM* –––, *T* ––––) to *TMSGZ*. The partially recessive alleles are all stable when carried in culture on glucose. That is, when glucose is the only carbohydrate in the culture medium, and the cells are not exposed to any other sugar, the cultures can be carried indefinitely in sub-culture without encountering any alleles except those of the original culture. Because of our experience with the mutagenic effect of saccharides on yeast, cultures in this Laboratory are never returned to the stored 'stock' cultures after having been grown on any sugar except glucose. The stock cultures are all grown on a complete natural medium of peptone and yeast extract. Mutations at the *TMSGZ* locus occur when cultures carrying the 'partially' recessive alleles *TMSG* –, *TMS–Z*, *TMS* ––, *TM* ––– and *T* –––– (excluding the totally recessive –––––– allele) are planted densely on an agar plate containing melezitose. For example, if 10^8 *TMSG* – cells are spread on an agar plate containing melezitose, a small number, approximately 1×10^{-7} *TMSGZ* cells, are recovered. Thus exposure of the partially recessive *TMSG* – culture to melezitose transforms the *TMSG* – gene from a partially recessive to the *TMSGZ* dominant. The other partially recessive alleles also mutate to *TMSGZ* in the same circumstances. All the different partially recessive alleles (*TMSG* –, *TMS–Z*, *TMS* ––, *TM* –––, *T* ––––) when exposed to melezitose mutate to the same allele and only to this allele—the totally dominant *TMSGZ*[10].

I suggest that the receptor is a protein folded on the surface of the chromosome. The phenomenon of melezitose-induced reverse mutation suggests that, in the presence of melezitose, a defective element (which is inferred to be a 'false' fold in the receptor-protein) becomes folded into a functional pattern in the 'new' receptor protein, thus correcting the defect. It appears that, in the absence of melezitose, each receptor-protein folds in the same manner its 'parent' protein had originally folded and that the folding pattern of each of the alleles is hereditary.

The fact that melezitose is a chemical substance which induces a specific mutation specifies it as a transforming agent.

The 'Respreading' Experiment

The fact that reverse mutations from *TMSG* – to *TMSGZ* do not occur at a detectable rate on glucose supports the view that melezitose is the mutagenic agent. Confirmation of this view is derived from Newcombe's "respreading" experiment[11]: if a dense suspension of cells is planted on a melezitose-agar plate and the cells are respread four hours later (after about 2 divisions have occurred) the number of revertant colonies appearing on the respread plate is statistically equivalent to the number which appears on a control melezitose-agar plate on which the cells were not respread. If respreading is delayed for 10 hr. (after each colony contains many more cells) an increase in *TMSGZ* colonies is observed. The respreading experiment proves that the fermenter cells were not originally present among the glucose-grown cells planted on melezitose-agar. Hence, the reverse mutations were produced by contact with melezitose. (The failure to obtain an increase in the number of fermenter colonies if respreading is performed within 4 hr. is not due to the failure to break up clusters of cells. This was demonstrated by respreading mixtures of fermenter and non-fermenter cells at 4 hr. When plates are inoculated with artificial mixtures, an increase in the number of fermenters consistent with the number of divisions which has occurred is always observed, indicating that even the small clusters of cells break up easily[8].) These observations do not exclude the possibility that some undetectable reverse mutations may occur at a very low rate. For example, if the rate were 1×10^{-12}, it would be difficult to sample a sufficient number of cells to make the test. Replica plating experiments[3] showed that the 'spontaneous' frequency of back mutation of the partially recessive allele is less than 1×10^{-8}.

The fact that no change in the number of resistant colonies occurs in the first 4 hr., during which at least 2 divisions have occurred, indicates that the mutation does not usually occur in any of the four cells which are produced during the first 2 divisions. The mutations appear to be delayed until after several generations of contact with the mutagenic carbohydrate, suggesting that growth of the cell is essential to the occurrence of the mutation. Since it is inferred that the mutation is due to a change in the folding of a protein-receptor, these results suggest that the change can only occur during the formation of a 'new' receptor and that the 'old' receptor remains unchanged, even in the presence of melezitose.

The fact that melezitose has the capacity to direct the mutation of a defective into a normal gene means that melezitose is a transforming agent. This experiment shows that agents other than nucleic acids have the capacity to produce gene-transformations.

Synergistic Effect of X-rays and Melezitose on Gene Transformation

Cells carrying the totally recessive allele, designated by 5 dashes (– – – – –), do not respond to any of the five inductors by the production of the adaptive enzyme, melezitase, and are refractory to the mutagenic effect of substrate in the absence of auxiliary treatment. When the totally recessive allele is spread on an agar plate containing melezitose, revertant colonies are not recovered. If, however, the culture is treated with X-rays before spreading on melezitose-agar a few dominant *TMSGZ* colonies are recovered[5,10]. When the frequency of recovered colonies was plotted against the X-ray dose, it was found that the mutagenic effect was produced by a single 'hit'.

Size of an Element

The results were used as the basis for calculating the size of the 'target'[12] and the calculation indicated that the element had a molecular weight of from 15 to 60. The determination of target size at a level much below that of a single nucleotide indicates that this mutation is due to changes in items smaller than single nucleotides, and, hence, that the 'element' is not a single nucleotide.

Refractory (Stable) Nature of the *T* Pattern

The ultra-violet-ray experiments dealt with the induction of 'loss' mutations (*TMSGZ* mutated to – – – – –; the '*T*' pattern from '*T*' to '–'); conversely, the X-ray-melezitose experiments involved the 'gain' mutation from – – – – – to *TMSGZ*, presumably by remodelling of the '*T*' pattern from '–' to '*T*'. X-rays seem to alter the turanose pattern in some way which permits melezitose to induce the mutation from – – – – – to *TMSGZ*, in which the turanose pattern is changed from one which does not fit turanose to one which does. The X-ray experiments showed that the – – – – – allele was refractory to the transformation (– to *T*) by substrate alone and that a previous treatment with X-rays was required to produce the change. The turanose pattern is also more resistant to mutation by ultra-violet rays from *TMSGZ* to – – – – – (*T* to –) than any of the other patterns – –. The turanose pattern resists mutation in either direction.

The turanose pattern appears to be the basic pattern, and all the other patterns seem to have the turanose pattern as an essential component. If the ability to ferment turanose were the only criterion by which the genotypes of the locus were identified, this locus would appear to be extraordinarily stable and of extremely high penetrance. The fruitfulness of the present inquiry has arisen from the fact that many different means were available for identifying the different multiple alleles.

Characteristics of the Enzyme produced by *TMSGZ*

Cells containing melezitase act on the five inductors immediately at different rates. In general, the adapted cells act most rapidly on turanose, next most rapidly on maltose; the rate on sucrose is slightly lower. The rates on alpha-methyl-glucoside and melezitose are much lower than the rate on sucrose. Although individual determinations are subject to some error, the lowest rate appears to be that on melezitose. This is true whether whole cells or cell-free preparations are tested; the similarity between cell-free preparations and whole cells excludes the possibility that the differences

in rates might be due to differences in the permeability of the membrane to the different saccharides.

The Permeability Barrier

Data from two sources revealed that the different inductors enter the cell at the same rate. (1) Data on oxygen absorption of a *TMSGZ* culture in solutions of the different sugars supported the view that the different rates of fermentation were not due to different rates of entry[4]. When curves, describing the rates of oxygen absorption of the cells undergoing adaptation to the sugars in different Warburg vessels, are extrapolated, they intersect on the time axis at the same point. Thus, the period elapsing from the time at which substrate is added to the time at which the cells respond is the same for the different substrates, indicating that the time required to pass through the permeability barrier is the same irrespective of the inductor. But the rate of fermentation of each substrate is characteristically different and this is inferred to be due to characteristic differences between the rates at which the same enzyme splits the different substrates. (2) Data from cell-free preparations (in which permeability barriers have been destroyed) confirmed the fact that the different rates after adaptation are due to the differences with which the induced enzyme acts on the different inductors.

A POSSIBLE MECHANISM OF GENE ACTION

Parallels between the Enzyme and the Receptor

It is generally held that the enzymes which act in the cytoplasm, and are produced in the cytoplasm, are proteins. Thus, the enzyme, melezitase, which is assumed to be a protein, acts with different rates on the different inductors, cleaving each inductor at a specific and characteristic rate. The rates may be arranged in the descending order: turanose, maltose, sucrose, alpha-methyl-glucoside and melezitose. There is a significant parallel between: (1) the activity of the enzyme toward the different substrates and (2) the sensitivity of the different patterns to ultra-violet rays. The correlation between these two different phenomena invites the hypothesis that both the receptor of the gene-system and the enzyme are folded proteins which mimic the topology of the surface of the carbohydrate inductors. The capacity of the single *TMSGZ* conformation to fit the five different inductors is inferred to be due to the relationships of the basic turanose pattern to the overlapping and partially superimposed patterns of the other four inductor molecules. The argument that the receptor surface is *not* deoxyribonucleic acid (DNA) is supported by the fact that nucleic acid is not needed to transform the defective surface into a functional surface since the trisaccharide, melezitose, can transform any of the impaired or damaged surfaces, presumably by acting as a model on which a new receptor surface is formed.

Relation of DNA to the Locus of the Gene

The hypothesis that the receptor is a folded protein does not rule out the essential involvement of nucleotides in the gene-system. It is proposed that the receptor 'fits' the chromosome by being engaged to the coded nucleotides, either RNA or DNA, which comprise the chromosome at the specific locus of the gene. This theory rejects the view that the chromosome is simply a double helix of DNA. It proposes that the chromosome is a many-stranded structure with both protein and RNA associated at the locus. It also proposes that if coding of the nucleotides has significance, some single strands of DNA must be free to react at the locus of the gene. On this theory, the specific variations of the outer surface of the receptor depend partially on the contact of the inner surface of the receptor with the single strands of coded nucleotides, and the integrity of the receptor depends on contact with these coded nucleotides. Minor deviations in the shape of the receptor which depend simply on folding of the protein may be independent of the nucleotide sequence and may be corrected by refolding the protein in the presence of the carbohydrate inductor. (These are the partially recessive mutations which can be induced to undergo mutation to normal by treatment with the inductor.) But if the nucleotides are rearranged, the surface of the conformation, and hence the patterns which fit the inductor, are disturbed. Reactions which affect the synthesis of purines or pyrimidines could produce gene mutations by altering the 'seat' on which the receptor is folded. The coded sequence of the nucleotides at the locus is essential to the maintenance of the conformation characteristic of the receptor surface because it would determine the type of folding which will occur, thus affecting the outer surface of the receptor. The theory is consistent with the view that changes in the nucleotide arrangement of the chromosome could lead to mutation.

On this hypothesis DNAase should destroy transforming principle, since it would remove the DNA 'seat' on which the protein is folded and maintained in the normal conformation. Re-arrangement of nucleotides in the chromosome would tend to change a normal gene into a defective gene.

The theory proposes that the receptor-protein has: (1) an outer (functional) surface and (2) an inner surface in contact with the nucleotides. The fact that the partially recessive alleles are transmitted unchanged from generation to generation suggests that irregularities in the folding of the receptor-protein, such as those, for example, which differentiate *TMSGZ* from *TMS* – –, are transmitted from generation to generation. This phenomenon suggests that hydrogen bondings within the folded protein are transmitted from generation to generation. It is proposed that this effect is produced by the folding of the 'new' protein produced at each 'new' generation on the lateral surface of the 'old' protein. In the presence of melezitose the receptor-protein occasionally folds on both the nucleotide surface and the melezitose surface and the irregularities in folding which produced the partially recessive alleles are 'corrected' and *TMSGZ* is produced.

Relation of Synapsis to Transformation

I have discussed elsewhere[13] the importance of DNA in homologous synapsis and proposed that the DNA component of the transforming principle ensures that the 'transforming agent' will be fitted into its proper position in the chromosome by combining with the homologous complementary single strands of DNA on the chromosome.

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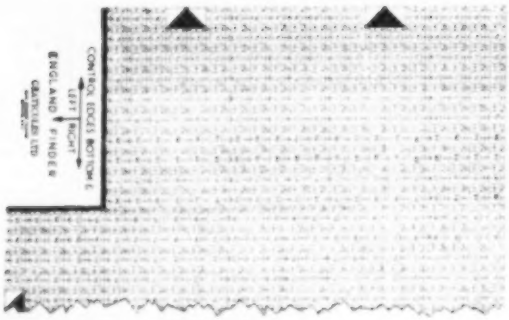

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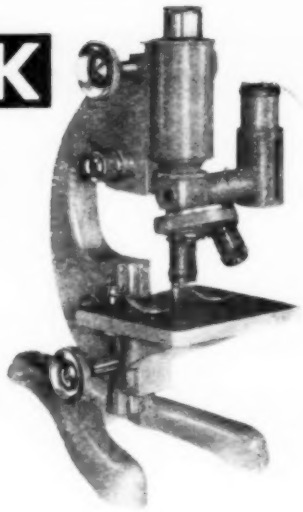

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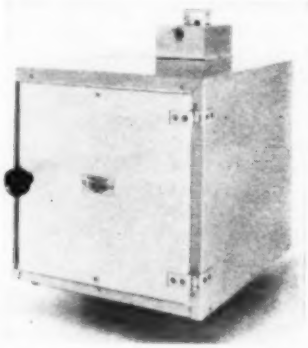

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The Particulate Gene

This theory implies a return to the theory of individual particulate gene and rejects the idea that genes are continuous[14]. The coded nucleotide serves: (1) to hold the receptor-protein in place; (2) to form a base on which the protein can fold in such a way that a functional conformation will result; and (3) to ensure the precise homologous synapsis which will prevent non-reciprocal or unequal crossing-over. On this theory, the gene is defined as a 'linear section of the chromosome capable of accommodating one species of a variety of closely related (allelic) receptors'. Steffensen's[15] theory of crossing-over, which states that the chromosome is a continuum in which nucleic acid segments are held together by Ca bonds, and that crossing-over occurs only at these Ca bonds, is consistent with the theory.

Crossing-over versus Other Kinds of Recombination

Crossing-over is defined as exchange occurring between chromatids by breakage and reunion which is usually reciprocal and is assumed to occur at the Steffensen bonds. Other kinds of recombinations may be due to gene changes by: (*a*) substitution, deletion or chemical alteration of nucleotides; (*b*) gene-conversion, gain or loss or alteration of receptor-protein; or (*c*) transduction. A critical discrimination between crossing-over and recombination due to causes other than crossing-over can be made only if tetrad analysis is available. Most of the low-frequency recombinations which have been revealed by viral and microbial genetical analysis are almost certainly not due to crossing-over.

Function of the Nucleolus

On this theory one element of the transmittor of each gene-system is the moiety of RNA[16] (the template) which passes from the nucleus into the cytoplasm to effect the synthesis of enzyme in the cytoplasm. The nucleolus is a temporary organelle appearing in a restricted region of a chromosome during the interphase between nuclear divisions. It is reasonable to suppose that the nucleolus is an organelle in which RNA is processed during its passage into the cytoplasm. The nucleolus affords an isolated site in which RNA could be altered without interfering with other reactions, especially reactions that occur in the cytoplasm. Thus the nucleolus would be an important component of the transmittor, and all that is known concerning the function of RNA in the synthesis of protein is consistent with the theory in explaining the synthesis of enzyme.

Gene-Conversion and Delayed Mutation

This theory suggests that the mechanism of gene-conversion might be different from that of transformation. Conversion from defective to normal, or *vice versa*, might occur in the heterozygote without breakage of the DNA strand of the chromosome and without involving crossing-over. It is proposed that conversion could be effected by the transfer of receptor-protein from the locus on one chromosome to the corresponding locus of its homologous partner. The stability of non-reciprocal recombinants in yeast heterozygotes[17] and the photo-reversibility of non-reciprocal recombinants[18] offer evidence in support of this hypothesis. Transfer of receptor-protein between homologous loci could produce the non-reciprocal recombinations detectable by tetrad analysis which are characteristic of gene-conversion. The stability of the multiple alleles produced by gene-conversion at meiosis suggests that only a few receptors are present on the meiotic chromosome. But it would be reasonable to suppose that many receptors are present at each locus of the mitotic chromosome. This could explain delayed mutations, because if a large population of receptor-proteins at a locus were predominantly normal, with only a few defective, many multiplications might occur before a gene containing predominantly defective receptors were produced. Variations in the penetrance, expressivity or potency of genes (or high rates of mutability) might be due to variations in the population of receptor-proteins at a locus.

Significance of the Parallel between Enzyme and Receptor

The new phenomenon revealed by the study of the *TMSGZ* alleles is the parallel between the properties of the receptor on the chromosome and the properties of the proteinaceous enzyme in the cytoplasm. The *TMSGZ* gene-system is identified by five characteristics: the ability to hydrolyse the five sugars—turanose, maltose, sucrose, α-methyl-glucoside and melezitose. Treatment of the cells with ultra-violet rays shows that the different patterns of the receptor vary in sensitivity to ultra-violet rays: the most sensitive pattern is the melezitose pattern; the most resistant pattern is the turanose pattern. The different patterns can be arranged in descending order according to ultra-violet sensitivity: *T*, *M*, *S*, *G* and *Z*. The changes in the gene are transmitted according to the rules of Mendelian heredity, proving that the experiments on sensitivity to ultra-violet rays pertain to the effects on the receptor located on the chromosome. But the characteristics of the enzyme involve events in the cytoplasm and the enzyme exhibits certain characteristics which parallel those of the gene. The substrates can be arranged in the following descending order according to the activity with which the enzyme acts on them: turanose, maltose, sucrose, α-methyl-glucoside and melezitose. The phenomenonological parallel between ultra-violet sensitivity of the patterns on the chromosome and the activity of the cytoplasmic proteinaceous enzyme suggest the possibility that both the receptor and the enzyme are protein. If the receptor-protein on the chromosome and the enzyme-protein in the cytoplasm are similar, the synthesis of enzyme in the cytoplasm involves a replication of the structure of the receptor in the cytoplasm. But this process must involve many intermediary steps because the synthesis of enzyme occurs in the cytoplasm far from the locus of the gene, where the induction occurred, and the protein itself does not pass from the nucleus into the cytoplasm. The biological economy achieved by constructing both receptors and enzymes from amino-acids probably lies in the fact that a pool of twenty activated amino-acids can serve as a source of protein which can be folded into almost any conceivable shape.

Mechanism of Gene Action

Enzymes are supposed to split carbohydrates by possessing a surface which almost fits the carbohydrate. If a disaccharide such as turanose impinges upon the enzyme surface it is subjected to distortion because the 'fit' is not perfect. This leads eventually to splitting the disaccharide into its two hexose components. The present theory of protein synthesis proposes that proteins are synthesized in the cytoplasm by the alignment of a series of activated amino-acids on a ribonucleic acid template[18]. The ribonucleic acid template assembles the amino-acids into a protein which is the enzyme. The ribonucleic acid template is a crucial component of the transmittor of the gene-system.

I shall propose that the RNA template arises from the locus of the gene on the chromosome. On this hypothesis there are some exposed nucleotides of single-stranded DNA available at the locus which bind RNA and receptor-protein to the locus. Double helices of DNA may also be present to give the chromosome structural integrity, but it is single-stranded DNA which is associated with the RNA and the receptor. At each locus the structural DNA is held in its place in the linear continuum of the chromosome by a calcium bond at each end. The locus is also occupied by an RNA nucleotide, corresponding in length and in the distribution of similar or complementary nucleotides with those of the DNA chain. But the RNA chain is not bound into the long axis of the chromosome by calcium bonds. The DNA-RNA-protein-receptor complex becomes unstable when the inductor unites with the receptor-protein and the RNA-template is released from the complex. Because the RNA-template is not calcium-bonded it is free to leave the locus and travel to the nucleolus, where it is processed for its passage through the nuclear membrane and its action in the cytoplasm.

POSSIBLE ORIGIN OF MENDELIAN GENES FROM ENVIRONMENTALLY ACQUIRED CHARACTERS

Origin of Adaptive Enzyme-forming Systems

I have suggested that the genome 'stores' the capacity to produce adaptive enzymes. The preceding hypothesis concerning the mechanism of gene-action may form a basis for a hypothesis concerning the origin of gene-systems. On this hypothesis, eobionts, which resembled the cytoplasmic-like coacervates conceived by Oparin[19], grew on the accumulated organic material which had been produced by abiotic syntheses, using (at one time) simple monosaccharides as energy sources. As the available monosaccharides became exhausted, accumulation of non-utilizable substances, such as disaccharides, intruded into the eobiont. The presence of the disaccharides impinging on the proteins, being formed by the eobiont, led to the construction of imperfect mirror images of the disaccharides by the same processes which lead antigens to initiate the construction of antibodies in the presence of unfolded proteins[20]. The imperfect fit to the surface of the disaccharide might produce a state of stress in the disaccharide molecule, causing the molecule to split and making a new source of energy in the form of monosaccharides available to the eobiont. The released 'enzyme' could then repeat the process. The disturbance produced by the disaccharide would lead to a temporary modification of the eobiont. So long as the 'enzymes' persisted a 'lingering modification' like that suggested by Jollos[21] would persist. The enzymatic process might have a very low rate, but in the absence of other sources of energy the rate would not be important. For many millennia energy might have been provided from new sources by this adaptive mechanism. Eventually some of the protein may have folded simultaneously, both on a ribonucleic acid and a saccharide, and the RNA would form a template for synthesis and folding of more enzyme, thus giving the eobiont an advantage, especially because replication of the nucleic acid might take place according to the Watson-Crick[22] hypothesis. A mechanism for replication of the template would reduce the time of adaptation by a large factor. Perpetuation of the enzyme in the cytoplasm would be assured, and the survival value of the virus-like RNA-cytoplasmic-template would increase the chances of survival of the eobiont.

But the theory thus far does not mention a nuclear apparatus. I have proposed that the genome is a recent development[23,24]. Hence, it remains to suggest a mechanism by which the capacity of the cytoplast to produce enzyme might have become stored in the genome. If DNA were available in the eobiont, or in its vicinity, a pattern reflecting the pattern of the cytoplasmic RNA might be present in the DNA. (It is assumed that these events may have occurred long before the origin of nuclei or cells, when the eobiont was only a slimy plasm.) If the nucleotides in the DNA were so arranged that the RNA template of the enzyme could become attached to the DNA by hydrogen bonds, the enzyme, carried by the RNA to the DNA, would become the protein-receptor of the chromosomal gene. The DNA-continuum would provide a locus on which the RNA-enzyme complex could be held in place and on which the RNA-template could duplicate the 'receptor-enzyme'. If this triple complex were supplied with the necessary materials for its continued replication, and if it could be isolated from the rest of the plasm, a genome capable of bringing forth the production of enzyme in the cytoplasm on contact with appropriate substrates would be established in the eobiont and might be expected to be maintained even during periods when no substrate was available.

Relation of Acquired Characters to Genes

The purpose of this article is to suggest the possibility of relating environmentally acquired characters to Mendelian genes. A hypothesis is presented which suggests that capacities to produce enzymes, acquired by the cytoplasm, eventually may become Mendelian genes. Unless the first eobiont carried the total potential exhibited by the great variety of living things, both past and present, it seems reasonable *a priori* that acquired characters must have become genic characters. Since no other hypothesis relating environmental modifications (acquired characters) to genes has been proposed, this hypothesis must serve to fill a void in theoretical biology until it can be replaced by one more acceptable.

This work has been supported by a research grant from the U.S. Public Health Service, *C4682*.

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OBITUARIES

Prof. Maud Menten

MAUD MENTEN, experimental pathologist, died on July 20, 1960, at the age of eighty-one in Leamington, Ontario. She was born in Lambton County, Canada, in 1879 and received the B.A. degree at the University of Toronto in 1904, the bachelor of medicine degree in 1907 and her M.D. in 1911. In 1916 she obtained a Ph.D. degree in biochemistry at the University of Chicago, where she studied with A. P. Mathews. Between 1904 and 1905 she was a demonstrator in physiology in the laboratories of A. B. Macallum. During 1907–8 she was a Research Fellow at the Rockefeller Institute for Medical Research, and, together with Simon Flexner and J. W. Jobling, was author of the first monograph of the Institute, a work on radiobromide and cancer. During 1910–12 and 1913–14 she was a Research Fellow at Western Reserve University in the sphere of Dr. George Crile. In 1913 she worked with L. Michaelis in Berlin, and this collaboration resulted in the famous paper on chemical kinetics which appeared in 1913 in the *Biochemische Zeitschrift*. In 1915–16 she did research in cancer at the Barnard Skin and Cancer Hospital in St. Louis, Missouri. In 1916 she joined the School of Medicine of the University of Pittsburgh, Pennsylvania, where she remained until her retirement in 1950. In Pittsburgh she was pathologist to the Children's Hospital of Pittsburgh from 1926 until 1950, and was a full-time teacher in the Department of Pathology of the Medical School; she rose to become a full professor of pathology. On retirement, she continued to do research work on cancer at the Medical Research Institute of British Columbia, until ill-health forced complete cessation of scientific activity in 1955.

Maud Menten was an avid research worker all her life. In Pittsburgh, despite full schedules as a hospital pathologist and teacher of pathology, she continued to make noteworthy contributions to scientific literature.

She was a versatile scientist, as becomes a pathologist. She will be best remembered at present for four pieces of work. Her work on enzyme kinetics with Michaelis in 1913 resulted in the Michaelis–Menten constant. In 1924, together with Helen Manning, she discovered the hyperglycæmic effects of salmonella toxins. In 1944, together with Andersch and Wilson, she determined the sedimentation constants and electrophoretic mobilities of adult and fœtal carboxylhæmoglobin; this has been stated to be the first use of electrophoretic mobility to determine differences in human haemoglobin, antedating Linus Pauling. In 1944, together with Junge and Green, she developed an azo-dye coupling reaction for the demonstration of alkaline phosphatase in the kidney. This piece of work was called enthusiastically "a stroke of genius" by A. G. Pearse in the first edition of his book on *Histochemistry* because it opened up a field of enzyme histochemistry. Other research papers encompassed work on potassium in cells (with A. B. Macallum), radiobromide and cancer (with Simon Flexner and J. W. Jobling), oxidases, vitamin C (with C. G. King and O. Bessey), streptococcal toxins, histochemistry of glycogen, and nucleic acids in bone marrow. Other papers were published in the fields of physiology, chemotherapy, haematology and pathology.

Dr. Menten was a member of numerous scientific societies. Aside from science, she was a student of languages, music and art. She was a fine painter, and several of her canvases were hung in art exhibitions.

Maud Menten was untiring in her efforts on behalf of sick children. She was an inspiring teacher who stimulated medical students, resident physicians and research associates to their best efforts. She will long be remembered by her associates for her keen mind, for a certain dignity of manner, for unobtrusive modesty, for her wit, and above all for her enthusiasm for research.

AARON H. STOCK
ANNA-MARY CARPENTER

Prof. G. Bonnier

PROF. GERT BONNIER died on January 11 in Stockholm, where he had held the chair of genetics from 1936 until 1958. Even after his retirement he continued his experimental work until a few days before his death. He belonged to the generation of geneticists who, under the influence of the Morgan school, started to analyse the mechanism of heredity by means of experiments with *Drosophila*. One of his earliest papers, published before he had obtained his doctorate, is a thorough and ingenious study of secondary non-disjunction, which may gain renewed importance now that non-disjunction in man has proved to be a source of profound pathological disturbances. Crossing-over in triploids and attached *X*-chromosomes, chromatid interference, gynandromorphism and mosaicism were among the problems that interested him most. In 1947, together with B. and M. Rasmuson, he published a paper on "Gene Divisibility", which at the time of its appearance

was somewhat of an oddity, but which now fits beautifully into the modern concept of the structure of the gene. After the War, Bonnier became increasingly interested in the genetical effects of X-rays and published a series of papers on this subject, several of them in collaboration with K. G. Lüning, his successor to the chair. Perhaps the most interesting result of these studies was the finding that X-rays produce more mutations in spermatozoa when they are exposed in the inseminated female than when the male is treated. During the past few years, Bonnier's interest in radiation genetics shifted from these more fundamental aspects to the problem of radiation damage to populations, and he studied the genetical effects of X-rays in model *Drosophila* populations of different breeding structures and under different selection pressures. All these investigations are characterized by carefully thought-out and often novel techniques, by large and painstakingly collected data, by thorough statistical analyses and by cautious and critical interpretations.

To geneticists in general, Bonnier is probably best known as a pioneer in applied genetics. In 1928, he became the first chief of the Animal Breeding Institute in Wiad; he held this position until the Wallenberg Fund in 1950 withdrew its financial support. There he introduced the use of cattle twins for systematic studies of the effects of environment and nutrition on identical genotypes; similar groups of twins have now been collected and are being studied at many research stations throughout the world. He was also one of the pioneers of the use of artificial insemination in cattle, and the centre organized at Wiad in 1936 was the first of its kind in Scandinavia.

As a person, Bonnier was modest and shy, full of kindness and tolerance, and with a quiet sense of humour; he was respected by all who came in contact with him and loved by many friends and pupils. His father had owned one of the largest publishing houses in Sweden, and the tradition of culture and gracious living in which he had grown up was continued in the life of his own family. To have been a visitor in his beautiful house and to have enjoyed the warm hospitality of him and his wife is an unforgettable memory. His death will be deplored not only as a loss to genetics; it will also be a deeply felt personal loss for many people in many countries.

CHARLOTTE AUERBACH

NEW FELLOWS OF THE ROYAL SOCIETY

AT a meeting of the Royal Society on March 16, the following were elected to fellowship of the Society:

PROF. J. BADDILEY, professor of organic chemistry in the University of Durham, King's College, Newcastle upon Tyne, distinguished for his researches in organic and biochemistry, particularly in the field of coenzymes, nucleotides, and bacterial cell-wall constituents.

PROF. H. E. M. BARLOW, dean of the Faculty of Engineering, and Pender professor of electrical engineering and director of laboratories in the University of London, University College, distinguished for his work on engineering aspects of microwaves, particularly wave guides and semiconductors.

PROF. M. S. BARTLETT, professor of statistics in the University of London, University College, distinguished for his contributions to the methods of mathematical statistics and their application to physical and biological science.

PROF. R. E. BILLINGHAM, professor of zoology in the University of Pennsylvania, Philadelphia, distinguished for his studies on the pigmentary system of mammals and on tissue transplantation.

PROF. C. C. BUTLER, professor of physics in the University of London, Imperial College of Science and Technology, distinguished for his researches on the elementary unstable particles in cosmic rays.

DR. J. CHATT, head of the Inorganic Chemistry Department, Akers Research Laboratories, Imperial Chemical Industries, Ltd., Welwyn, Hertfordshire, and group manager of the Heavy Organic Chemicals Division, distinguished for his work on the chemical and physical constitution of co-ordinated metallic compounds.

PROF. B. H. FLOWERS, Langworthy professor of physics in the University of Manchester, distinguished for his numerous contributions to theoretical nuclear physics, especially the shell model of the atomic nucleus.

DR. L. H. GRAY, director of the British Empire Cancer Campaign Research Unit in Radiobiology, Mount Vernon Hospital and Radium Institute, Northwood, Middlesex, distinguished for his contributions to the effects of radiations on cells and to radiotherapy.

DR. S. H. HAUGHTON, inter-African scientific correspondent for geology, Commission for Technical Co-operation in Africa, Pretoria, formerly director of the Geological Survey of South Africa, distinguished for his many contributions to South African geology, especially in the fields of palæozoology, stratigraphy and economic geology.

PROF. RODNEY HILL, professor of applied mathematics in the University of Nottingham, distinguished for his contributions to the theory of continuous mediums, particularly to the plasticity of metals.

DR. H. E. HINTON, reader in entomology in the University of Bristol, distinguished for his work on insect biology, particularly on the larval stages of insects, and on classification and morphology of Coleoptera, Lepidoptera and Diptera.

DR. R. G. S. HUDSON, Research Fellow in the Department of Geology, Trinity College, Dublin, distinguished for his stratigraphical and palæontological researches in the Carboniferous of the North of England and in the Mesozoic rocks of the Middle East.

MR. C. F. KEARTON, managing director, Courtaulds, Ltd., Coventry, distinguished for his work on chemical engineering characteristics of volatile uranium products and for technological development in the textile industry.

Dr. H. London, deputy chief scientific officer at the Atomic Energy Research Establishment, Harwell, distinguished for his work on superconductivity, on liquid helium, and on the separation of isotopes.

Prof. M. Maizels, professor of clinical pathology in the University of London, University College Hospital Medical School, distinguished for his investigations into the mechanisms by which the electrolyte composition of animal cells is maintained.

Prof. Irene Manton, professor of botany in the University of Leeds, distinguished for her studies on the ultramicroscopic structure of plants and for studies on their evolution.

Dr. L. Marion, senior director, National Research Council of Canada, and director, Division of Pure Chemistry, Ottawa, distinguished for his work in organic chemistry, particularly in the field of alkaloids.

Prof. A. A. Miles, director of the Lister Institute of Preventive Medicine, London, and professor of experimental pathology in the University of London, distinguished for his contributions to bacteriology, and for his work on the mechanism of inflammatory reactions.

Prof. D. G. Northcott, Town Trust professor of pure mathematics in the University of Sheffield, distinguished for his work in abstract algebra and its application to algebraic geometry.

Dr. G. J. Popjak, director of the Medical Research Council Experimental Radiopathology Research Unit, Hammersmith Hospital, London, distinguished for his work on lipid metabolism and for elucidating the biosynthesis of fatty acids and cholesterol.

Dr. J. A. Pople, superintendent of the Basic Physics Division of the National Physical Laboratory, Teddington, Middlesex, distinguished for his work on the application of quantum mechanics to the explanation of the chemical and spectroscopic properties of molecules.

Dr. R. N. Robertson, executive of the Commonwealth Scientific and Industrial Research Organization, Melbourne, and professor designate of botany, University of Adelaide, distinguished for his contributions to plant physiology, particularly on salt accumulation and respiration and the ripening of fruits.

Dr. S. Siddiqui, director of the Pakistan Council of Scientific and Industrial Research, Karachi, distinguished for his work in the chemistry of natural products and for his leadership in the promotion of research in Pakistan.

Prof. A. W. Skempton, professor of civil engineering in the University of London, Imperial College of Science and Technology, distinguished for his pioneering work on soil mechanics, particularly in relation to the shear strength and other physical properties of clays.

Prof. M. J. D. White, professor of zoology in the University of Melbourne, distinguished for his contributions to animal cytology, particularly in relation to evolutionary processes.

NEWS and VIEWS

International Control of Investigations of Rare Meteorites

In recent years the study of meteorites has rapidly increased and, in the hands of investigators such as Urey, Anders, Wiik, Vinogradov and others, has thrown much light on the composition and origin of the solar system and of the planets. Last year, through the work of Mason on hydrous silicates in meteorites, interest has concentrated on the rarest form of meteorites, those which contain carbonaceous material. It follows from Mason's results, as well as from the earlier analyses of carbonaceous material by G. Mueller, that carbonaceous meteorites, unlike all other types, had never been subjected to high temperatures since their formation and that they might well contain samples of the raw materials from which life may have been formed on larger planets. On March 16, this hypothesis was given a new turn by the announcement at the meeting of the New York Academy of Sciences that Prof. B. Nagy, Dr. W. Meinschein and Dr. D. Hennessy had, by using mass spectroscopic and X-ray methods, found in the carbonaceous material from the meteorite which fell near Orgeuil in France on May 14, 1864, paraffinoid hydrocarbons characteristic of living organisms and hence had, in the opinions of these investigators, provided proof for the existence of life on its presumed parent body. This view is unlikely to go unchallenged, but whatever the final consensus of opinion, the crucial importance of this study of the carbonaceous meteorites is now evident.

The great publicity deservedly given to these observations and deductions has focused the attention of scientists in many countries on the carbonaceous meteorites. Paradoxically, the result may well be, unless appropriate steps are taken in time, to bring the researches to a rapid end by destroying the irreplaceable material on which they are based. There is known to be only some 30 kgm. of well-attested carbonaceous meteorites in museums. More, but not much more, may be in the hands of dealers or may be brought to light in other ways. Already these rare bodies are being examined in a dozen or more laboratories, each with a different objective and by methods which render the material useless for further study. This can only result in the exhaustion of the stock unless prompt measures are taken to ensure intranational and international co-operation similar to that in the various sections of the International Geophysical Year in the analysis of meteorites by different but complementary methods. The appropriate body for this is clearly the Committee on Space Research of the International Council of Scientific Unions, which, by a slight extension of its terms of reference, might cover bodies coming in from outer space as well as those going out into it. It is hoped that at the forthcoming meeting of the Committee at Florence, the matter can be discussed and

appropriate measures taken in time to secure that the maximum of information is obtained from meteorites with the minimum of destruction.

Mathematics at Hull : Prof. G. C. Steward

This year Prof. G. C. Steward retires from the chair of mathematics in the University of Hull. He has occupied this chair since 1930, soon after the University College was first established. On his retirement, separate chairs of pure and applied mathematics are being instituted. Prof. Steward had his degree studies interrupted by the First World War, and he did not finally graduate at Cambridge until 1920. He was joint winner of a Smith's Prize in 1922. Meanwhile, he spent three years as assistant lecturer at Leeds before returning in 1923 to Cambridge as fellow and mathematical lecturer at Emmanuel College. He went directly from Cambridge to Hull. In 1918 he worked in the optics division of the National Physical Laboratory. This determined the course of his research work, which has been mainly on optical systems, using the eikonal function of Bruns, and other methods. He is the author of a Cambridge tract on symmetric optical instruments. In recent years he has been increasingly involved in departmental organization.

Prof. W. H. Cockcroft

Dr. W. H. Cockcroft, who is to be the first holder of the chair of pure mathematics in the University of Hull, was one of Prof. J. H. C. Whitehead's research students in the immediate post-war period. Since his doctorate at Oxford he has taught at the Universities of Aberdeen, Chicago and Southampton, where he is now a reader. His scientific interests are naturally directly derived from his early work under Whitehead. He was concerned in the first instance with various algebraic questions about group extensions and with some special problems arising in homotopy theory. He has since made contributions to homological algebra and topology generally. To mention one or two examples of research work of his, one may refer to some work which he and R. G. Swann have done in making improvements in the algebraic machinery used in Whitehead's work on simple homotopy types. In his work on the cohomology groups of a fibre space he has analysed the methods of the Belgian topologist Hirsch. In particular, he has obtained an explicit form for Hirsch's coboundary operator. This enables Cockcroft to make improvements in his own earlier work as well as to explain some results of Eilenberg–Maclane. Cockcroft has also taken great interest in the teaching of mathematics to undergraduates, and has taken part in symposia throughout the United States on the invitation of the National Science Foundation.

Prof. N. B. Slater

Dr. N. B. Slater, who has been appointed to the newly created chair of applied mathematics in the University of Hull, studied at the Universities of Edinburgh and Cambridge. For the year 1939–40 he was an observer at the Solar Physics Observatory, Cambridge; for the rest of the war years he was a member of Prof. L. Rosenhead's team in the Projectile Development Establishment. Since 1945 he has been on the applied mathematics staff of the University of Leeds, successively as lecturer, senior lecturer and reader. His Cambridge appointment led to a strong interest in amateur astronomy. It also led to an acquaintance with Sir Arthur Eddington, and, after the latter's death, Slater was asked to go through his unpublished manuscripts. He found that these cast a vivid light on the development of the ideas in Eddington's *Fundamental Theory*, and described what he found in a book published in 1957. However, Slater's main research interest has been in the theory of unimolecular gas reactions, on which he first began work under R. H. Fowler before 1939. In this field he has produced a standard theory, which has attracted a good deal of attention. A course given while visiting Cornell University was expanded by him into a book on the subject, which was published in 1959.

The National Reference Library for Science and Technology

In an adjournment debate in the House of Commons on March 14, Mr. A. Albu asked a number of questions regarding the National Reference Library for Science and Technology. Stressing the value to the research worker of the open access system in the Patent Office Library, he questioned the adequacy of the proposed book stock of 500,000 current volumes, and thought that comparison with similar libraries elsewhere suggested a stock twenty times that proposed. He asked for specific assurances that the non-current volumes to be transferred to the British Museum would be readily available, that the site provided adequate room for expansion, and that measures were being taken to recruit staff of appropriate high scientific calibre. The Parliamentary Secretary for Science, Mr. D. Freeth, in his reply, said that it is not anticipated that there will be any overlapping or confusion of responsibility, although the Library will be part of the British Museum Library and come under the Chancellor of the Exchequer and not the Department of Scientific and Industrial Research and the Minister for Science. It will occupy a site to the east of the southern approach just north of the existing Cornwall Hall, and it is considered that the Library's total area of about 130,000 sq. ft. is well suited to house the 500,000 volumes required to provide the complete reference desired, together with an expert staff and open access. Reading rooms totalling about 22,000 sq. ft. will seat about 300 with seating room for a further 300 among the book stacks. The total cost is estimated at about £2·5 million.

Mr. Freeth said that the site does not provide room for all the expansion that might be desirable in future, but it is believed that it will provide a worthy national reference library, and that it will be possible to provide a speedy and adequate system for research workers to procure earlier publications from the British Museum. Legislation will be necessary for this purpose. The present stock of the Patent Office Library amounts to 210,000 volumes of periodicals, 100,000 volumes of patent specifications and 70,000 text-books; more than 7,500 current periodicals, including 300 Russian, are taken. Expenditure in 1960 was just under £180,000 and the staff numbered 72. Building plans have already reached an advanced stage, and Mr. Freeth said that any suggestions which prospective users might have for this building should be sent to the Principal Keeper in the Department of Printed Books in the British Museum, London, W.C.1, or to the Librarian, Patent Office Library, 25 Southampton Buildings, London, W.C.2. The exact constitution of the advisory committee to be set up when the new Library comes into operation

is not yet decided. The Government is determined to see that the Library has an adequate expert staff; there will be ample provision for photocopying, and the new Library will co-operate fully in research into information techniques.

Nestor: a New Reactor at Winfrith

A NEW 10-kW. reactor, *Nestor*, was put into operation for the first time at the Atomic Energy Establishment, Winfrith, on March 13. Its purpose is to act as a source of neutrons for sub-critical assemblies of nuclear fuels and moderators. The reactor core, control gear and instrumentation were designed and installed by the Hawker Siddeley Nuclear Power Co., which modified the design of its *Jason* reactor to enable up to five sub-critical assemblies to be driven simultaneously by the reactor. This concept represents a major advance in the use of a reactor as a neutron source. The Turriff Construction Corporation, Ltd., was responsible for the installation of the special shielding and the civil work generally. The nuclear fuel in *Nestor* is an alloy of highly enriched uranium and aluminium in the form of aluminium clad plates arranged in an annulus around a graphite cylinder, and natural water is used both as coolant and moderator. The reactor is provided with control and safety rods, and additional control is possible by varying the water-level. The experimental assemblies will be placed in 'caves' formed in the shielding at the sides and above the reactor. The whole shielding is arranged to be demountable so that the caves can be rebuilt to accommodate major changes in the requirements of the experimental programme.

The reactor is capable of operation at 10 kW. (heat), giving a thermal neutron flux of 10^{11} neutrons/cm.^{2}/sec. in the centre of the core and of up to 10^{8} neutrons/cm.^{2}/sec. in the sub-assemblies. The thermal neutron flux for each sub-critical assembly can be varied by altering the reactor power-level, by using neutron shutters or by rearranging the fuel loading in the annular core.

Netherlands Atom Forum

A NUMBER of Netherlands industries together with the Reactor Centre of the Netherlands have taken the initiative for the establishment of the 'Netherlands Atom Forum'. The object of the new body is to give publicity to the developments in the field of nuclear energy, in particular to the activities in this domain, of the Netherlands industry and of institutes engaged in the subject. The intention is to do this by means of publications, the organization of conferences and information meetings, and the co-ordination of Netherlands participation in exhibitions. The Forum will also attend to the documentation and information on the development and application of nuclear energy, if possible in co-operation with existing organizations at home and abroad. It will in future represent the Netherlands in the 'Forum Atomique Européenne', which was established in Paris on July 12, 1960, and in which corresponding organizations from other Euratom countries, as well as from non-Euratom countries, have been brought together. Mr. W. A. de Haas, secretary of the Industrial Commission of the Reactor Centrum Nederland, has been elected chairman of the Netherlands Atom Forum; the secretariat is accommodated at Reactor Centrum Nederland, Scheveningseweg 112, Den Haag.

Sea-water Purification Unit based on New Principles

A NEW type of evaporator developed for sea-water by the General Electric Co. of America may have application to other forms of heat exchangers, particularly because of the greater heat transference it achieves per unit area. The basis of its present form is a conventional steam-jacketed vertical copper tube 50 in. long and 6 in. diameter, from which evaporated vapour leaves at the top and concentrated brine at the bottom. The novel feature is the addition of wiper blades on a hollow shaft which sweep the inner surface of the tube at a speed of 300 ft./min. and spread sea-water issuing from the shaft and a header as a film some 0·001 in. thick on the wall. The tube is 0·05 in. thick and fluted lengthwise externally to provide increased heat exchange surface and improved removal of condensate; together with the wiper action heat transfer-rates of 40,000 B.TH.U./sq. ft./hr. can be obtained without perceptible carry-over of spray. It is claimed that with a throughput evaporation of 40 per cent a purity of one part of salt per million is achieved. The makers expect to realize a saving in weight and space of some 40 and 60 per cent, respectively, over conventional plants and have in mind systems evaporating 1,000–1,000,000 gallons daily.

Arts Graduates and Imperial Chemical Industries, Ltd.

A NOVEL method of directing attention to the opportunities existing at Imperial Chemical Industries, Ltd., for arts graduates is set out in an attractive handbook (*A Degree nearer Industry*. Pp. 40. By Kenneth Harris (London: Recruitment Section, Imperial Chemical Industries, Ltd.), 1960). Kenneth Harris, a well-known industrial journalist, was invited to carry out a survey of his own devising to find out what had happened to arts graduates in the different companies of the Imperial Chemical Industries, Ltd., during recent years. The report prepared by Harris is frank and not always complimentary to Imperial Chemical Industries, Ltd., but clearly shows that here is a company where young men of the right qualities are needed and can find their way to the top. The booklet could well be read by all arts graduates contemplating a career in industry—the picture painted by Harris is not dissimilar from that of many other large industrial organizations.

Durban Museum and Art Gallery

THE report of the Durban Museum and Art Gallery for the municipal year 1959–60 records the development of the new Marine Gallery on modern museum lines, and pleads once again for new buildings for both the Museum and Art Gallery (Pp. 20. Durban: Durban Museum and Art Gallery, 1960). A large and varied selection of temporary exhibitions were staged during the year and the collections at the Old House have been expanded and their display considerably improved.

British Technology Index

IF sufficient support is forthcoming, a new endeavour is to be made to index the contents of British technical periodicals. There have been at least two earlier attempts to do this, and it is probable that part of the reason for their failures was the absence of a cumulative index or volume. The new *Index* will have 11 monthly parts (no August issue)

and a bound annual cumulation. It will be sponsored by the Library Association and will index about 400 journals, many of which are not already abstracted or indexed. It will produce each issue within six weeks of the publication of the journals concerned. The price will be about 15 guineas. Further particulars, and a prospectus containing a specimen page, are obtainable from the Association at Chaucer House, Malet Place, London, W.C.1.

Field Studies Council

That the Field Studies Council is performing a real service to learning is again clearly brought out in its annual report for the year 1959–60 (Pp. 32 + 4 plates. (London: Field Studies Council, 9 Devereux Court, W.C.2.) 1961). Between 1951 and 1960 the number of visitors to the centres has more than doubled and, in 1960, was well over 8,000. It is interesting that more than half the visitors went to study 'biological subjects', and more than 3,000 studied 'geographical and geological subjects'; only 315 students were concerned with the 'countryside and natural history subjects'. The figures reflect mounting pressure from grammar schools and training colleges, while the report indicates that the centres could have been filled many times over between March and Whitsuntide. During the year amenities at Slapton Ley were improved and the new geography block was completed at Dale Fort.

The World Meteorological Organization: 1961 Events

The World Meteorological Organization has announced its schedule of conferences and symposia to be organized during the rest of 1961: April 12–26, Commission for Hydrological Meteorology—first session (Washington); June–July, Regional Association III—South America—third session (Rio de Janeiro); August 6–12, international symposium on "Atmospheric Ozone and General Circulation", to be held in conjunction with the International Ozone Commission (Arosa); August 14–19, symposium on "Radiation", to be held in conjunction with the Radiation Commission of the International Association of Meteorology and Atmospheric Physics (Vienna); September 18–October 2, Commission for Aerology—third session (Rome); October 2–7, symposium on "Climatic Changes", to be held in conjunction with Unesco (Rome). Further information can be obtained from the Secretariat, World Meteorological Organization, Geneva.

The Night Sky in April

Full moon occurs on April 1d. 05h. 48m. U.T., new moon on April 15d. 05h. 38m. and full moon on April 30d. 18h. 41m. The following conjunctions with the Moon take place: April 9d. 06h., Saturn 3° S.; April 9d. 14h., Jupiter 3° S.; April 18d. 13h., Aldebaran 0·4° S.; April 22d. 05h., Mars 5° N.; April 25d. 05h., Regulus 1° N. In addition to these conjunctions with the Moon, Mercury is in conjunction with Venus on April 18d. 01h., Mercury being 9° S., and Mars with Pollux on April 23d. 03h., Mars being 5° S. Mercury is too close to the Sun for easy observation. Venus will be visible for a few days at the beginning of the month as a bright star low in the west after sunset, but later in the month it is too close to the Sun for observation. Mars sets at 2h. 50m., 2h. 20m. and 1h. 40m. on April 1, 15 and 30, respectively. Mars is an evening star, but conditions for observation are becoming less favourable. Its stellar magnitude on April 15 is + 1·1; its distance is rapidly increasing and its apparent diameter decreasing. Jupiter and Saturn are morning stars, both rising just over two hours before the Sun; conditions for observation are not favourable. There is one occultation of a star brighter than magnitude 6 during the month, observations being made at Greenwich: Aldebaran, disappearance April 18d. 12h. 24·3m., reappearance April 18d. 13h. 01·4m. The Lyrid meteors are active during April 20–22, the maximum being on April 22. The radiant is at R.A. 18h. 04m., Dec. + 33°, and conditions for observation are very favourable.

Announcements

Prof. Dragoslav Popovic has been appointed director of the International Atomic Energy Agency's Safeguards Division, in succession to Mr. R. M. Smith (Canada). Prof. Popovic is at present at the Boris Kidric Institute of Nuclear Science at Vinca, near Belgrade, and has been professor of nuclear reactor engineering at the University of Belgrade since 1958.

Dr. Karl F. Meyer, director emeritus and professor emeritus of the University of California's George Williams Hooper Foundation for Medical Research, has been awarded the Jessie Stevenson Kovalenko Medal of the U.S. National Academy of Sciences. The award has been made in recognition of Dr. Meyer's achievements as an investigator, teacher and administrator in medicine for more than half a century, and especially for his work on the role of animals as hosts for vectors of human disease.

The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., with the aid of a grant from the Population Council, is continuing its post-doctoral programme for scientific training in reproductive physiology. Fellowships will be awarded to candidates possessing the Ph.D. or M.D. degrees, or their equivalents; they will carry a stipend of 5,500 dollars per annum and will be for a twelve-month period. Application forms can be obtained from Dr. Celso-Ramon Garcia, at the Worcester Foundation, and should be returned not later than June 1.

The British Hydromechanics Research Association is organizing an international meeting on "Fluid Sealing" at Grosvenor Hall, Ashford, Kent, during April 17–19. Further information can be obtained from Mr. H. Stephens, information officer, British Hydromechanics Research Association, South Road, Temple Fields, Harlow, Essex.

A symposium on "The Water Relations of Plants" is being organized by the British Ecological Society, and will be held at the Imperial College of Science and Technology, London, during April 5–8. Further information can be obtained from Dr. F. H. Whitehead, Botany Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7.

The ninth annual general meeting and conference of the British Agricultural History Society is to be held at Seale Hayne Agricultural College, Newton Abbot, Devon, from the evening of April 5 until lunch-time April 7. Further information can be obtained from Mr. S. T. Morris, 1 Courtenay Park, Newton Abbot, Devon.

HISTORY AND PHILOSOPHY OF SCIENCE IN THE COMMONWEALTH

By Dr. W. MAYS

Department of Philosophy, University of Manchester

The General Problem

THE history and philosophy of science is a subject of increasing importance, both in the universities and outside them. In the universities, where the division between the sciences and the humanities is growing more acute, it has a most valuable part to play. By integrating diverse fields of study, it can do a great deal to ameliorate the evils of over-specialization.

Because of this it seemed worth while finding out how the subject was developing in the British Commonwealth universities, both in its teaching and research aspects. These universities form a fairly coherent unit, since, in most cases, they have been founded on the model of the British universities. To obtain this information, a questionnaire was sent out to a hundred universities, most of which were in Australia, Canada, India and South Africa. Out of these, thirty-nine reported activity in the history and philosophy of science, and to this information was added returns from twenty-one British universities[1].

Six groups of questions were asked: (1) was the university teaching the history and philosophy of science as a regular and independent part of the curriculum; (2) whether there was an established post or the expectation of one; (3) the type of course given; (4) the manner of treatment; (5) the value of the subject; (6) general remarks.

Value and Future of the Subject

Most of the replies stressed the value of the subject in university curricula. In the case of science students such courses were seen as a means of integrating knowledge of the physical world with the humanities and as a counter to specialization. So far as arts students were concerned, it was thought that courses of this sort enabled them to obtain a general scientific outlook, and made them conversant with the influence of science on philosophy and culture.

In most Commonwealth universities very few independent teaching appointments have as yet been made. Most of the lecturing appears to be of a stop-gap variety carried out by members of science, philosophy or education departments. What clearly emerged was that the most effective way of teaching the subject was through an autonomous department. In a modern university unless a subject has departmental independence and representation on the governing academic body, its chances of internal growth may be slight. Melbourne, the only Commonwealth university outside Britain to have an autonomous department, was firmly convinced of the benefits accruing from its independent position. It is also clear that in view of its importance, both as a subject in its own right and as an integrating discipline, there is a very strong case for the establishment of chairs in the history and philosophy of science, at least in the larger universities.

The following points were also made. More university teachers in the subject were needed: (*a*) for research, and (*b*) for undergraduate teaching. There was a need to include the history and philosophy of science as part of the general education of sixth-form pupils as well as undergraduates. As the demand for the subject in schools will probably expand, it would be useful to have courses in education departments for prospective teachers of the subject. Further, there would seem to be important teaching possibilities in the field of extra-mural studies.

Results of the Survey

In Great Britain the Universities of London, Oxford and Cambridge have well-established teaching and research departments. The oldest department is that of the History and Philosophy of Science at University College, London, founded nearly thirty years ago. It is, however, mainly concerned with postgraduate studies. Another London department is that of Philosophy, Logic, and Scientific Method at the London School of Economics, where both undergraduate and graduate courses are given. The Oxford and Cambridge Departments are more recent and are post-Second World War creations. At Cambridge, the history and philosophy of science may be taken as an optional half-subject in the Natural Sciences Tripos, and a certificate in the subject is also awarded. Oxford provides an extensive range of courses and awards a diploma. Research degrees may be taken at London, Oxford and Cambridge.

Aberdeen has a reader in the history and philosophy of science. In some modern universities a number of lectureships as well as extra-mural posts have been established. At others the subject is taught by scientists, philosophers or education department staffs. In Great Britain there is, as yet, no established honours school in the history and philosophy of science; but, in view of the value of the subject, it seems desirable that such a school be set up in the near future in one or more of the British universities.

The Australian universities are well ahead in the history and philosophy of science. Some of them are large in size, and they may have felt the need to introduce the subject in an attempt to solve problems relating to the integration of university studies. The Melbourne Department has a staff of six and two part-time tutors, and awards both honours and research degrees, as well as providing courses for other departments. Queensland and Sydney both have an established lectureship in the history of science. The Australian National University, Canberra, is contemplating making an appointment in this field.

Even among the smaller Canadian universities there seems to be an interest in the subject. In some of the university medical schools a course in the

history of medicine is offered. At McGill University there is an established chair in the history of medicine, and Assumption University, Windsor, Ontario, has a professor of physics and the philosophy of science. There do not, however, seem to be any postgraduate or graduate degrees or diplomas available for interested students.

The overall picture in South Africa, at the moment, is that there are neither independent departments nor teaching posts. A fair amount of teaching is done by members of science departments, and there are a number of compulsory courses given at different universities. One University, Witwatersrand, apart from providing courses in the history and philosophy of science for B.Sc. students, has recommended the establishment of a teaching post.

Indian and Pakistani universities use the subject mainly for giving science students a historical background, and for broadening the interests of arts students. It is taught by lecturers in science and philosophy. Finally, there is a group of widely scattered universities and colleges—West Indies, Ibadan, Rhodesia and Nyasaland, and Hong-Kong—at which some instruction in the subject may be obtained. Out of these Hong-Kong seems to be the only one contemplating a separate course in the history of science.

[1] Mays, W., *Brit. J. Phil. Sci.* (November 1960).

THE CARNEGIE INSTITUTION OF WASHINGTON

ANNUAL REPORT

YEAR Book No. 59 of the Carnegie Institution of Washington* covers the year ended June 30, 1960, and includes the report of the president, Dr. Caryl Haskins (see *Nature*, March 4, p. 695), reports of Departments and Special Studies, as well as the administrative reports of the Executive Committee and the Auditors, and list of publications during the year. In his review of the year, Dr. Haskins again emphasizes the extent to which the growing-points of science arise at the line of contact between disciplines or depend on theoretical studies for guidance, so that fundamental and applied science really form a continuum. Growing-points have been particularly noticeable during the year in geophysics, the observation of outer space and of the stellar universe and in the study of the cellular structure of life and of its nature at the molecular level, and in all these fields the research workers of the Institution have contributed towards the understanding of our beautifully intricate and orderly world.

At the Mount Wilson and Palomar Observatories a cluster of galaxies, which are apparently receding from the Earth at about 138,000 km. per sec., was photographed with the 200-in. Hale telescope, and the cluster proved to be a strong source of radiation, particularly at the longer wave-lengths. It is estimated that the cluster is eight times as distant as the colliding galaxies in Cygnus *A*, and it is certainly several thousands of millions light-years distant from the Earth. Continued exploration of the interior of the Earth by the Geophysical Laboratory yielded results suggesting that the sharp transition in rock composition at some 400 km. below the Earth's surface may be at least partly due to a transition from one mineral form to another occurring naturally under the conditions of temperature and pressure at that depth. At high temperatures and pressures of 60,000–80,000 atmospheres, the iron–olivine fayalite has been metamorphosed into a dense spinel form, and since the olivines are very generally distributed within the Earth's crust and mantle, a transition from natural olivine to spinel may be a significant change associated with the structural discontinuity observed seismically at 400 km. Another feature of the year's work in this field was the synthesis of diamonds, while the opportunities implicit in the existence of the five independent nuclear age-dating methods continued to be explored, and new information was obtained which may help to resolve problems arising from the lack of agreement of ages obtained from zircon with those obtained from micas. A significant advance in the study of metastable phases and their relation to polymorphic transformations in sulphide minerals is noted, and an attempt to understand the structural mechanism of high-order transitions led to the conclusion that a mixed crystal is not a homogeneous edifice.

In the Department of Terrestrial Magnetism, a new 60-ft. radio telescope was installed which will be used to measure hydrogen clouds in our own Galaxy, and duplicates of the Department's extended antenna arrays for studying the radio emission of the Sun have been provided for collaborators in Chile, the Argentine and Uruguay, and, with assistance from the National Science Foundation, a duplicate of the Department's equatorially mounted parabolic antenna is to be built in South America, probably near Buenos Aires. Stress is laid on the Department's participation in the International Geophysical Year and afterwards in the International Geophysical Co-operation; but a major part of the scientific effort of this Department continues to be devoted to biophysics, particularly the study of protein synthesis by bacteria and other simple forms of life. During the year, ribonucleic acid was extracted from ribosomes in a manner that preserves hydrogen and magnesium bonds, and a unit equivalent to ribonucleic acid in a large ribosomal particle was obtained which could be broken down into units one-twentieth to one-fortieth of their size. These units were isolated from living cells and occur naturally both in the ribosomes and in the non-particulate fraction of the cells, and it also appears that the large ribosomal units are formed in the growing cell by assembly of these subunits of ribonucleic acid and associated protein.

In the Department of Genetics, in work with the bacteriophage *T2*, which infects *Escherichia coli*, using chromatography on a column of basic protein, half molecules and quarter molecules of phage deoxyribonucleic acid have been identified, and the sedimentation coefficient and intrinsic viscosity of the quarter

* Carnegie Institution of Washington. Year Book No. 59: July 1, 1959–June 30, 1960. Pp. lvii + 515 + 25 plates. (Washington, D.C.: Carnegie Institution of Washington, 1960.) Cloth bound, 1.50 dollars; Paper bound, 1 dollar.

molecule point to a molecular weight of about 13 million. Evidence has also been obtained that formation of some proteins is at least linked with the development of phage deoxyribonucleic acid, and by comparing the effects of chloramphenicol when added at different times after the infection of bacteria with the *T2* phage evidence was also obtained suggesting a correlation of the evolution of the resistance to radiation with the synthesis of deoxyribonucleic acid. Other work in the Department suggests that even mild chemical agents of cellular origin have mutagenic activity. The enzyme deoxyribonuclease proved mutagenic to *Drosophila melanogaster* under laboratory conditions, treatment of larvæ and imagines with deoxyribonuclease producing both recessive and dominant lethal effects and chromosomal re-arrangement in the flies.

In the Department of Embryology, use of the techniques of rapid serial radiography and cinéradiography provided direct evidence that arterial blood enters the maternal placenta from the endometrial arteries under a pressure sufficiently high to drive it through the intervillous space and towards the chorionic membrane of the fœtus. Injection of radiopaque dyes into the femoral arteries of anæsthetized pregnant rhesus monkeys and observation of the course of the dyes by rapid serial X-ray photographs or by cinéradiography yielded films showing with great clarity the predicted characteristic spurts of blood as the dye enters the intervillous space. A major programme was completed in which chicken spleen was used to study the properties of immunologically competent tissues and the course of cells emanating from spleen grafts labelled with tritiated thymidine was traced within embryonic chick hosts. The cells of both donor and host appear to contribute to the spleen reaction, the host cells predominating numerically.

A new technique used during the year in the Department of Plant Biology facilitated the detection of the several forms of chlorophyll, and experiments with the algal genus *Phormidium* showed that the pigment phycoerythrin increased efficiency of light absorbed by chlorophyll *a* 695 and other forms of chlorophyll *a*. It also appears that a maximum rate of *Chlorella* photosynthesis is reached only when the two photochemical reactions initiated by the two parts of interdependent pigments are proceeding in the correct ratio. Studies of the amino-acids isolated from cultures of *Chlorella pyrenoidosa* and examination of their carbon isotope composition indicated that some of the amino-acids, such as leucine and valine, contain markedly less carbon-13 than is present in the inorganic environment, and while others, like serine, had ratios much closer to the inorganic carbon dioxide used as input, the carboxyl carbons of all chains contained a higher proportion of carbon-13 than the remainder of the carbon chains of the amino-acid. If it can be assumed that the isotope abundance found in the lipids or in the non-carboxylic portion of aspartic or glutamic acids in *Chlorella* is characteristic of the fixation of carbon dioxide in carbohydrates, a considerable fraction of the carbon fixed in *Chlorella* must be incorporated by pathways other than those traditionally described for photosynthesis.

Further progress is reported in the development of image tubes for telescopes, and while further technical refinement is still required to remove imperfections, thirty-fold reductions in exposure time have been obtained as compared with direct photography. Dr. Haskins's review directs special attention to a report by Dr. F. Chayes, of the Geophysical Laboratory, "Correlation in Closed Tables", included in that Department's report, as an example of uncommitted research in the Institution. The research was stimulated by certain problems in petrography, but has novel and potentially useful conclusions applicable to the statistical analysis of data obtained in many branches of experimental science.

TECHNICIANS IN ENGINEERING AND CHEMICAL INDUSTRIES IN BRITAIN

THE results of a sample survey of the employment of technicians in the engineering and chemical industries, carried out in 1960 by the Ministry of Labour, are analysed in the *Ministry of Labour Gazette* of December.

Replies received from 309 of the 400 firms approached, of which three-quarters employed more than 1,000 workers and the remainder 100–999, indicated that in most groups the percentage of qualified scientists and engineers to the total number of employees is a little higher than the corresponding percentages obtained from the survey of scientific and engineering man-power made at the beginning of 1959. Technicians formed 8·7 per cent of all employees of the firms included in the survey, the figure varying from 11·6 per cent in the electrical engineering group to 4·1 in the 'other metal goods' group. Except in the chemical and allied industries, few women technicians were employed, the proportion for all groups being 4·6 per cent, and for the chemical and allied industries 10·4 per cent; in the latter group, 34 per cent of the women were employed in research and development laboratories and 54 per cent on testing, inspection and analysis.

In the chemical and allied industries the proportion of technicians to qualified scientists or engineers was 1·6 : 1, compared with 4 : 1 in electrical engineering and electronics, and 7·6 : 1 in motor-vehicles and aircraft. The average ratio for all groups was 4·2 : 1, but the inquiry confirms that for engineering industries as a whole 5 or 6 technicians are required for each technologist. In all but the chemical group of industries the shortage of technicians in January 1960, measured by the percentage of vacancies that occurred at the time to the total number of technicians employed, was rather less serious than the shortage of qualified scientists and engineers a year earlier. The forecast demand for technicians in the two years following the survey was in most groups about twice the number of vacancies occurring. Over the whole field, the largest number (32·7 per cent) of technicians was employed in the design and drawing office, and 29·1 per cent of all technicians

were design assistants or draughtsmen, testing, inspection and analysis accounting for 14·4 per cent.

Design and drawing office work accounted for 40·7 per cent of all vacancies for technicians (67·5 per cent in shipbuilding and marine engineering firms), but in the chemical industry 44·6 per cent of vacancies were for laboratory technicians for research and development. An analysis of requirements for the next two years presented a similar picture. In the chemical group of industries 63 per cent of technicians had some qualification, and this group employed 43 per cent of all technicians with the General Certificate of Education at Advanced Level, while in the shipbuilding and marine engineering industry 58 per cent of technicians had a qualification. About 10 per cent of all the firms referred to apprenticeships, technician, student or drawing office combined with courses at technical colleges for which release on one day a week was granted, but nearly 70 per cent replied that no courses of instruction were provided.

HEALTH OF BRITISH SCHOOL CHILDREN

"THE great majority of school children are not only robust and healthy, but are taller and heavier than their predecessors", states Sir John Charles, the chief medical officer of the Ministry of Education, in his report for 1958 and 1959*.

Sir John says under-nutrition has almost disappeared in Britain, and the differences between the heights and weights of children in good and poor districts are lessening. More fat than under-nourished children are being reported, but the number in each group is small.

Only about five per cent of school children contracted a notifiable infectious disease in the years under review. Tuberculosis continued to decline. Poliomyelitis reached its lowest level for thirteen years, and vaccination against it was undertaken vigorously everywhere. There were local outbreaks of diphtheria that involved 47 school children in 1958, of whom five died; seventy-seven were affected in 1959 with no deaths. Advocating the continued need for immunization the report directs attention to the fact that "as recently as twenty years ago 55,000 persons contracted diphtheria annually, of whom almost 3,000 died".

The main cause of death among children is through accident. More children aged 5–15 years die from accidents than from all congenital malformations and of circulatory, genito-urinary infections and respiratory diseases altogether. In 1958, 869 children of 5–15 years died from accidents, including 395 from accidents involving motor vehicles, 174 from drowning, and 58 from burns and scalds; 113 fatal accidents took place in the home.

The second chief cause of death of children of this age-group is cancer. There were 499 deaths in 1958, mainly from leukæmia. Other causes were respiratory diseases, 253; congenital malformations, 185; infectious diseases, 137; genito-urinary diseases, 76; and only 53 from diseases of the heart and blood vessels. More children died from appendicitis (44) than from rheumatic fever and rheumatic heart disease (30); these conditions were once widespread and deadly. The report stresses the need for unremitting research into the causes of the so-called congenital diseases and defects. "Medical research gives us reason to believe that some diseases that we consider hereditary or congenital in origin may well be found to be due to adverse influences in pregnancy or infancy." These diseases and defects cause the death each year of about 4,000 children under the age of fifteen years and leave thousands disabled. To this must be added those who are mentally retarded or who are blind or deaf from birth or early infancy. Although most children are healthy and without blemish, there are tens of thousands who are disabled to a greater or lesser degree.

The report welcomes the increasing number of education authorities which are considering, or who have already started, a modification of the fifty-year old system of periodical medical examination. In these areas all children will be examined after first starting and before leaving school; but, instead of a periodical examination of intermediate age-groups, doctors will visit the schools more frequently and give more attention to the new children who appear to need it. The hope is expressed that school doctors will be able to give more time to the study of particular diseases and disabilities as they affect children at school. Illustrations given are respiratory diseases—as many as 100,000 boys and girls have asthma some time during their childhood—and the nature and effects of skin diseases, from which tens of thousands of children are still reported to be suffering.

In 1958 more than two million children were examined at periodical school medical examinations. More than 809,000 were examined in schools and clinics at the special request of the parents, doctors, nurses, teachers, or others, and nearly 1,044,000 were re-examined for defects found at a previous examination. The comparable figures for 1959 were 2,138,000; 704,000 and 1,041,000.

About 15 out of every 100 children who were examined after first starting school were found with some defects which required treatment; in some areas, from one in five to almost one in two of these were not receiving it. Often the parents did not know of the defect or did not appreciate its significance. Prevalence of defects found at periodical inspections shows that 175,000 are treated annually for skin diseases; 200,000 orthopædic defects, mostly slight; 15,000 boys and girls are under treatment for epilepsy; 2,000 boys and girls of school age have diabetes. There are fewer children with heart disease. Of every thousand boys and girls examined, twelve had a heart defect in 1958 compared with eighteen in 1948. The recorded prevalence of lung disease in school children has become almost stationary since 1948. Of every thousand children examined 24 were found with lung disease in 1948 and 25 in 1958.

Although the number of verminous children is still "deplorably high"—219,000 in 1958 and 223,000 in 1959—it is less than half the figure of 464,000 in 1948.

* The Health of the School Child: Report of the Chief Medical Officer of the Ministry of Education for the years 1958 and 1959. Pp. iii+231+8 plates. (London: H.M. Stationery Office, 1960.) 10s. 6d. net.

A small number of children attend school inadequately clad. There is, however, widespread comment about the unsuitable types of shoes worn by many children, especially older girls. A school doctor in Hertfordshire reported that younger children were well shod, but that "many girls of secondary school age would not be guided otherwise than by the dictates of fashion".

The report says that it is doubtful whether children will refrain from smoking so long as they see their parents and teachers enjoying the habit. A survey of about 3,500 boys and girls in two grammar schools and four modern secondary schools in a county borough near London shows that eight per cent of the children are 'regular' smokers—the smoking of five cigarettes a week being defined as regular for the purposes of the survey. One third of the children aged 14–16 who are 'regular' smokers smoke more than twenty cigarettes a week. Another survey carried out in Oxfordshire of about 8,300 children shows that nearly 1,600 are smokers and spend £4,350 a year on cigarettes. Nearly half these children say that they have heard that there is some connexion between cigarette smoking and lung cancer.

The report emphasizes that, generally, facilities are adequate for medical treatment, but are seriously inadequate for dental treatment; the national shortage of dentists is the main deficiency. The school dental service is able to treat only a little more than half the number of children who require treatment. A large number, many of whom attend non-maintained schools, are treated by the general dental service, but hundreds of thousands are neglected.

In 1959, for the first time, the number of part-time dentists did not balance the number of whole-time dentists who retired or who left the service.

Special surveys of the teeth of the 5–12 year old children in eight representative areas show that deterioration of the teeth was less in five-year olds, but greater in twelve-year old children between 1953 and 1958 than between 1948 and 1953. "It is significant that during the period 1948–1958 sugar consumption per head in the United Kingdom rose from 88·3 lbs. in 1948 to 103·1 lbs. in 1953 and 120·7 lbs. in 1958", states the report.

The report of the working party set up in 1949 "to direct and organize an investigation on the prophylactic effects of the local application of a solution of fluoride to school children's teeth", is published as an appendix to the report. The working party considers that the application of a fluoride solution to the teeth is not a worthwhile preventive measure in the conditions of the investigation, that is, when the treatment is given on a wide scale in the public dental service. This may well enhance the interest already being taken in alternative methods of caries prevention, such as fluoridation of drinking water and the dental health education of the public, and especially children, in such matters as proper diet and the cleansing of teeth.

A notable feature of the work of the School Health Service in the years under review is the increased attention given to children with emotional or behaviour problems, and also of those with speech defects, but there was a serious shortage of child guidance clinic staff and of speech therapists. Much attention was paid to handicapped children; 54 new special schools, with accommodation for 5,732 children, were opened in 1958 and 1959, bringing the total number of handicapped children in special schools to more than 60,000. Much interest, too, was taken in children with defective hearing, and an increasing number of local education authorities employed peripatetic teachers of the deaf to visit children in ordinary schools, or opened special classes in ordinary schools for partially hearing children. During this period a large number of the new Medresco transistor hearing aids were supplied to school children.

Sir John insists that a school health service cannot ignore the challenge of children from problem families, of those who have been before the courts, or of promiscuity among some older adolescents. These boys and girls formed a small minority of the school population, but they presented "a tough problem to the medical, education and social services—three services that must work together".

Appendixes to the report include, in addition to the usual statistical tables, a list of the research projects being undertaken in the school health service and an index to *The Health of the School Child* for the period 1935–57.

STRENGTH AND PROPERTIES OF TIMBER

RESEARCH into timbers is undertaken in England at the Forest Products Research Laboratory, Princes Risborough, and is under the auspices of the Department of Scientific and Industrial Research. *Forest Products Research Bulletin* No. 45, entitled "The Strength and Properties of Timber", by F. H. Armstrong*, supersedes two earlier ones on the same subject and contains fresh material. Information on the properties of no fewer than 172 kinds of timber is presented in the proportion of some 37 home-grown timbers to 136 imported timbers, figures which may appear to some to be rather disproportionate, but the Laboratory has done a useful service to Commonwealth countries while not actually ignoring home-grown material, which has been handled more intensively. The technique of timber-testing has made considerable advances in recent years, and one new development in England has been the adoption of the 'Monnin' system, which makes use of 2-cm. square instead of 2-in. square test-pieces, and is thus more suitable for small-diameter trees.

The gist of this *Bulletin* consists of three tabular statements occupying about 16 pages. The physical and mechanical properties of home grown timbers are given in Table 1, those of imported timbers, based on 2-in. test-pieces, in Table 2, and those of imported timbers, based on 2-cm. test-pieces, in

* Pp. vi + 34 + 8 plates. (London: H.M. Stationery Office, 1960.) 3*s.* 6*d.* net.

Table 3. The contents of species in the last two tables do not conform. The data refer to the eight tests made, namely, six tests of physical properties, of (*a*) static bending, (*b*) impact bending, (*c*) compression parallel to grain, (*d*) hardness, (*e*) shear parallel to grain, and (*f*) cleavage, supplemented by physical tests of moisture content and specific gravity. These tests and the apparatus used are described in some detail with the help of photographs. Since the most important factors which influence the strength of a timber are its moisture content and specific gravity, these are dealt with in some detail. Regarding the latter, it appears that, in respect of the actual wood substance, it is for all practical purposes the same for all species, but that the amount of that substance varies with the species, so that there is, in fact, a wide variation of specific gravity, and strength, not only between different species but also within each species. The strength values given in the tables are primarily intended for a comparison of species. Here it must be pointed out that while the pieces tested may be representative of variation of the properties within individual trees or small groups of trees, they can scarcely be said to be fully, or even fairly, representative of any species for the whole range of conditions under which it is grown. The largest number of trees or planks tested refer to Weymouth pine (56), Corsican pine (38), beech (36) and Scots pine (35), whereas for some tropical species a single tree has provided all the test-pieces.

In this connexion the presentation of the data can be criticized on the grounds that the first letter of a name is not a good scientific basis for grouping, although it is admittedly useful in locating a species within a group. It does seem incongruous, for example, to find horse chestnut sandwiched in Table 3 between dahoma and North Bornean kapur. The grouping adopted here might have been taken a little farther; there would have been no disadvantage if the timbers of each country had been grouped together—in alphabetical order.

An interesting and unexpected feature of the *Bulletin* is an introduction to simple statistical methods useful in comparing results or testing relationships between variables, and justifiably applied here in handling the data from many samples from one tree or group of trees from one source. The recognition of the possible importance of such factors as capacity to resist fungous attack or the effects of atmospheric fluctuations seems to indicate a new outlook. The value of the graphs presented in Fig. 5, showing the relationship between specific gravity and maximum compressive strength, is much impaired by the absence of a key to link up the plotted numbers with the corresponding species.

This publication is a useful contribution to our knowledge of the properties of a wide range of timbers, many with very odd names, and it should be of value to importers and to timber-growers in Commonwealth countries who are endeavouring to find markets for so-called 'secondary' timber trees. To the layman it should convey some idea of the widely varying character of timber as a raw material.

DUCTILE BERYLLIUM

SOME fifty years of work on the production of ductile beryllium would appear to have come to full fruition by the announcement by the Chesterfield Tube Co., Ltd., a subsidiary of Tube Investments, Ltd., of its ability to supply this metal in a variety of sections, including finned tubes, with mechanical properties in the hot-extruded state, which include a tensile strength of 30–45 tons per sq. in. and an elongation in the longitudinal direction of 4–10 per cent*.

The problem of overcoming the brittleness of beryllium has been approached by controlling the purity of the metal, by reducing the grain-size and by control of the crystalline orientation. Although the two first avenues can exert beneficial effects, it is the last that, at present, offers the most promising line of attack. As a result of its hexagonal structure, beryllium shows marked anisotropy both of strength and ductility. At ordinary temperatures the main slip occurs on the basal plane and on the prism faces in the <1120> direction; the critical stress needed to initiate basal slip being about one-fifth of that on the prism face. Very little basal slip can, however, take place before fracture occurs, while quite extensive slip can occur on the prism face provided that the orientation is such that slip on the basal plane is inhibited. As the temperature is raised, the stress necessary to produce prismatic slip falls, and at 500° C. it is the same for both forms.

Mechanical operations such as rolling or extrusion result in a preferred orientation of the crystals to which hexagonal metals are particularly prone, whence the behaviour of extensively worked material approaches that of a single crystal. As a result, a tensile force applied normally to the basal plane results in a brittle fracture, but a force parallel to that plane leads to considerable ductility. In an extruded flat section, for example, the basal planes tend to lie parallel to the sides of the flat, the longitudinal ductility of the section being high, 5–15 per cent elongation, but transversely, the ductility may be negligible. The extrusion techniques which have now been developed control the orientation of the grains, so that in a tube the basal planes, instead of radiating from the tube axis, are randomly orientated over the cross-section. Bursting tests at 600° C. have shown 10 per cent expansion at failure for such randomly orientated tubes as compared with 2–4 per cent for tubes with the radial texture.

It would appear that, although beryllium with some degree of ductility has been known for some time, this is an important step forward which, moreover, may well have applications to other hexagonal metals, for example, magnesium.

* Chesterfield Tube Co., Ltd. Fabrication of Beryllium Tubes and Sections: a New Structural Metal with Unique Properties. Pp. 16. (Chesterfield: Chesterfield Tube Co., Ltd., 1960.)

DEPOSITION OF FISSION PRODUCT NUCLIDES AFTER TWO SAHARA NUCLEAR TEST EXPLOSIONS

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THE daily concentration of the radioactive dust particles as short-lived radium and thorium daughter products and long-lived fission products from nuclear test explosions in ground-level air have been estimated by the filter sampling method over several years[1]. Continuous measurements of the radioactive fall-out and rain-out in weekly and monthly intervals were added to the previous methods later[2]. The influence of two Sahara nuclear test explosions (on February 13 and April 1, 1960) on the fission product nuclides in the ground-level air in Czechoslovakia was not characterized by a sudden rise of fission product activity, but by a slow increase during the second quarter of the year 1960. The beginning of this increase appeared at the end of February. This observation is in satisfactory agreement with the simultaneous measurements of the radioactivity in the fall-out and rain. The increase of the fission product nuclides in the ground-level air in the mean monthly values is evident: the mean fission product activity during the second quarter of the year 1960 was about 320 per cent higher than that during the fourth quarter of the year 1959 (= 100 per cent); the latter was the lowest during the whole year 1959 as a result of the stopping of nuclear test explosions on November 1, 1958.

During March 1–17, 1960, the fission product content of rain-water presented several high peaks as a result of the first French nuclear test explosion. After April 8, 1960, a new increase in the fission product nuclides in rain-water was observed as a consequence of the second Sahara nuclear test explosion. The radioactivity deposited on a 1-m.^{2} area was, for example, on March 1, 1960, 42 times greater than on February 27, 1960. The fission-product activity in the rain-water after the second nuclear weapon test showed no further peaks after the first one and its activity was much lower. The increase in the rain-water activity as a result of two Sahara nuclear tests lasted until June 1960. An interesting result is demonstrated by the mean monthly fission-product activities in the rain-water expressed as specific activities of 1 litre rain-water: if the mean activity in January 1960 is regarded as 100 per cent, February shows 98 per cent, March 795 per cent, April 244 per cent, May 170 per cent and June 77 per cent. The activities of the rain-water deposited monthly on a 1-m.^{2} area were remarkable too: if the mean activity in January 1960 is regarded as 100 per cent, February was 53 per cent, March 1,360 per cent, April 455 per cent, May 186 per cent and June 132 per cent.

Moreover, the deposition of radioactive dust which is removed from the atmosphere by wash-out in rain-water and by dry deposition directly on to surfaces was observed at weekly and monthly intervals by the pot-method. The weekly fall-out radioactivity results are presented in the histogram (Fig. 1). Two peaks may be seen there, the first one in the tenth week (February 29–March 6, 1960), the second one in the fifteenth week (April 4–10, 1960), as a result of the second nuclear test explosion.

Fig. 1. Histogram of weekly deposited radioactive fall-out in the first half of the year 1960

Another method of autoradiographical research on the deposition of radioactive dust was tried in this laboratory independently of the macroscopical research methods described of observing fission-product nuclides in the ground-level air and in fall-out and in rain. This method rendered possible a microscopical observation of the deposited radioactive dust particles. For this purpose, glass plates (18 × 24 cm.) covered by a film of 'Vaseline' mixture were used. The sticky glass-plates were exposed for the deposition of the fall-out and rain in the free atmosphere for 14–21 days. Afterwards they were put for three days in a dust-free box for short-lived radium and thorium daughter products decay. Then the glass plates ready for autoradiography were covered with a thin plastic foil and pressed to a X-ray film (Agfa Laue film) for a longer period. The exposed X-ray film was developed in a hard-working developer.

The radioactive fall-out dust particles deposited, and fixed on the sticky surface, could be seen on the X-ray film after developing as dark centres of variable size and blackening. An interesting illustration of the quantity and quality of deposited radioactive fall-out dust particles on to the Earth's

Fig. 2. Autoradiogram of radioactive dust particles deposited from the atmosphere from March 7 to March 20, 1960, on a sticky glass plate

Fig. 3. Autoradiogram of radioactive dust particles deposited from the atmosphere from March 21 to April 10, 1960, on a sticky glass plate. It contains several 'hot' particles in consequence of the second Sahara nuclear test explosion

surface was given by the number and the blackening of centres.

Several glass plates exposed during the beginning of the year 1960, including that exposed in the ninth and tenth weeks (February 22–March 6, 1960), when a great peak in the weekly fall-out results was observed (Fig. 1), were not successful owing to a short autoradiographic exposure. The next glass plate exposed in the eleventh and twelfth weeks (March 7–20, 1960) gave an autoradiogram presented in Fig. 2. It contains only four radioactive centres of varying size and blackening. This result is in general agreement with the fall-out histogram in Fig. 1. The next glass plate exposed in the thirteenth to fifteenth weeks (March 21–April 10, 1960) is presented by its autoradiogram in Fig. 3. It gave a very clear result: it contains much deposited radioactive fall-out dust particles of different size and blackening. This autoradiogram demonstrates the presence and the deposition of a great mass of radioactive dust particles from the atmosphere, probably as a result of the second Sahara nuclear test explosion. This information is in good agreement with the second peak on the histogram in Fig. 1.

The further autoradiograms of glass plates, exposed in the free atmosphere in November 1960, contained several radioactive centres of small activities only. Thus the results described were verified, and an argument presented for a new purification of the atmosphere from the fission product nuclides in agreement with the results reached by other methods.

The deposited radioactive dust particles from the atmosphere create 'hot' particles with greater activity of the order 10^{-9} c. by agglomeration processes from smaller ones; several large centres in Fig. 3 may be due to 'hot' particles.

The concentration of fission product nuclides on dust particles has raised many new physical, biological and hygienic problems. As there is a possibility of inhalation of 'hot' particles or incorporation in some other way a radiobiological danger of irradiation arises, for example, on the endothelium of the bronchi.

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A RADAR OBSERVATION OF A SEA-BREEZE FRONT

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IN the course of an investigation of the origin of radar 'angels', an unusual line source of radar echoes was recorded. Photographic time-compression techniques enabled the development and progress of the line echo to be investigated in detail. The photographic techniques and the parameters of the 23-cm. radar installation used have been previously described[1–3].

Fig. 1 shows the line echo as it appeared on the radar plan position indicator at 1700 hr. (6 p.m. B.S.T.) at about its maximum intensity, the isochrones on Fig. 2 indicating its development and movement. The line first became evident at about 1200 hr. along the coast near Felixstowe; it then moved inland, increasing in intensity and accelerating gradually until sunset, by which time it had reached nearly 50 miles inland and was moving at 6 knots. A similar line developed over Kent and Sussex, moving inland in a similar way. The whole phenomenon decayed rapidly over the sunset period 1930–2000 hr.

Scintillating discrete angels could be seen breaking away from the line during its strongest period; on the eastern side of the northern segment over Hertfordshire and Suffolk, and from both sides of the Sussex segments of the line.

In addition to the line echo the screen was well covered with discrete angels during this day. Most were of the short-lived, or rapidly scintillating kind, and these showed no very obvious pattern of movement. However, a well-marked stream of persistent angel echoes could be seen moving up the Thames estuary, and some of these could be tracked for considerable distances, occasionally even across the line echo.

The development of the line at the coast and the speed and form of its movement inland suggest a sea-breeze effect, and this appears to be confirmed by the meteorological evidence.

On June 20, 1960, an anticyclone covered the country, and there was almost no cloud and little wind. The data of Table 1, taken from the Daily Weather Report, indicate the changes over the afternoon at some relevant stations.

Table 1

Station	1200 hr. (G.M.T.)				1800 hr. (G.M.T.)			
	Wind		Temp.(°F.)		Wind		Temp.(°F.)	
	Speed	Direction	Air	Dew pt.	Speed	Direction	Air	Dew pt.
Felixstowe	17 kt.	50°	66	49	13 kt.	60°	62	51
Mildenhall	3 kt.	20°	69	52	5 kt.	40°	70	44
Gatwick	9 kt.	350°	71	51	6 kt.	90°	75	56
Thorney Island	4 kt.	320°	73	45	2 kt.	200°	71	55

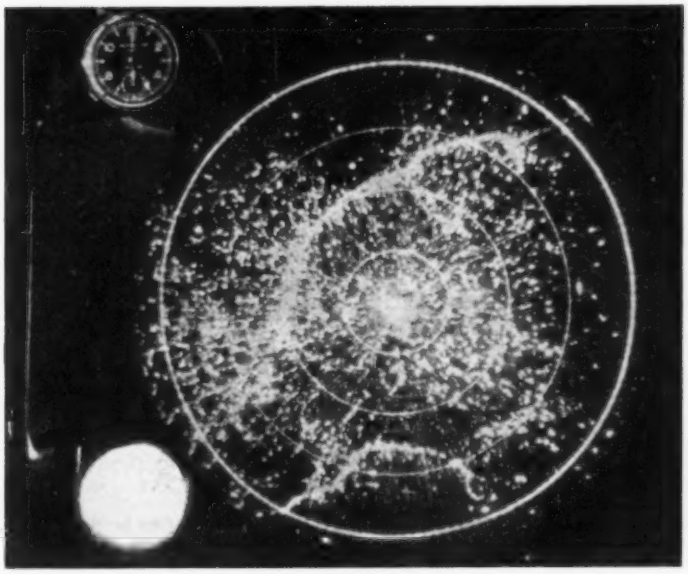

Fig. 1. Plan position indicator photograph, 1700 hr., June 20, 1960 (clock shows B.S.T.)

The line echo passed over Gatwick and would doubtless have been observed to pass over Thorney Island also if this station had been within range-setting of the radar display photographed. The changes in wind direction and in dew point at these two stations thus appear to offer good confirmation of the sea-breeze hypothesis.

It appears, then, that the radar was in fact seeing a remarkably well-developed sea-breeze front, for its maximum penetration inland was about 50 miles, while its greatest length, including both north and south segments, was little short of 120 miles.

It is of interest to consider the mechanism by which the radar energy has been reflected from the front. Cloud echo can be eliminated both by the plan position indicator appearance and by the 0/8 cloud reported by the relevant synoptic stations. The necessary echoing area must therefore be provided either by birds or by refractive index effects in the gaseous atmosphere. Formally, of course, both factors certainly contribute, and in this case it will be shown that each can make a significant contribution.

The discrete angel echoes moving away from the line echo have already been mentioned. They scintillate strongly, and move from the line at a velocity of about 30 knots, though the scintillation makes accurate measurement difficult. As discussed below, the frontal zone is a region of strong convection, so that soaring birds may well be present along the line echo, and may account for the angels breaking from it, since the velocities measured are of the correct order. A small flight of birds would provide sufficient echoing area to account for these angels, and if many such flights were air-borne, soaring in the frontal region, their resultant echo would present the continuous appearance seen, as in the case of the ring angels already shown to be due to starlings[2]. The sharp edge seen in the frontal echo is also evident in the rings.

We now consider the magnitude of the echoes to be expected from the refractive discontinuities.

Excepting the front under discussion, the synoptic situation was almost stationary throughout the day, and the radiosonde ascent from Hemsby at 1100 hr. gives adequately representative data. The atmosphere was very stable and abnormally dry to 1,400 m., and the refractive index profile shows a step discontinuity of 13 N units at this level ($N = (n - 1) \times 10^6$; n being the refractive index coefficient). The slope of the N profile is otherwise as for a standard atmosphere. The refractive index of the sea-breeze air may be estimated as follows. Air having the moisture content shown by Felixstowe at 1800 hr. (dew pt. 11° C.) and warmed to the temperature shown by Cardington (22° C.) is transported adiabatically to 1,400 m., at which height a difference of 30 N units is shown with the ambient air.

The frontal region is thus considered as a line of thermals rising to about 4,000 ft. In the absence of mixing the rising air differs from its surroundings by 30 N units at this level.

If this discontinuity can be considered sufficiently sharp, taking place, for example, in about 5 cm., then a plane reflexion coefficient :

$$\rho = \tfrac{1}{2} \Delta n \quad \text{may be used (ref. 4, p. 7)}$$
$$= 1{\cdot}5 \times 10^{-6}$$

If the beam is filled with such a sheet, from 4,000 ft. to say 1,000 ft. at ground cut-off, the signal received may be calculated to be 1 db. below the threshold of detection.

The actual target configuration is not a plane sheet, however, but numerous discrete thermals, rising somewhat 'doughnut' shaped; for example, as described by Scorer[5]. Each thermal thus presents

Fig. 2. Development of the sea-breeze front, June 20, 1960. Range ring 40 nautical miles. Surface winds: 1200 hr., short arrow; 1800 hr., long arrow

the discontinuity to the incident energy many times, and though the intensity of the reflecting boundary must decay due to mixing, there is also the possibility of focusing of energy from the rear surface of the thermal column. It appears quite possible that such thermals, probably filling the pulse volume in depth, may provide a returned signal greater in intensity than the hypothetical plane sheet used in calculation.

Rather similar line echoes have been reported by Atlas[6], and by Ligda and Bigler[7], each favouring a refractive explanation similar to that offered above. In the former case, using 1·25-cm. radar, the absence of birds was verified. However, Harper[8] has produced evidence in favour of soaring birds as the back-scatterers responsible for some line echoes of somewhat similar appearance.

In conclusion, we comment on the length and penetration inland of the sea-breeze front observed, and secondarily note that in this case it seems probable that both birds and refractive discontinuities have contributed to mark its passage.

We thank our colleagues, especially in the Radar and Photographic Groups, who made the observations possible.

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DIFFUSION THROUGH POROUS MATERIALS

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IT is often necessary to calculate the amount of a gas or vapour diffusing through a porous bed of material. The diffusion is less than that through the air because of the interposing solid portions through which, in general, there is virtually no diffusion. Usually an attempt is made to relate the ratio D/D_a to the porosity ε, where D is the diffusion coefficient for diffusion through the porous structure, and D_a is the corresponding coefficient through air. For example, in the later stages of the drying of thick porous structures the water surface retreats inwards and the falling rate of drying is maintained by the diffusion of water vapour from the surface of evaporation through a layer of the dry material. In calculating this diffusion, Nissan, Kaye and Bell[1] made the simple assumption that, with no diffusion through the solid, the area available for diffusion would be the average area of the air space, that is, εA, where A is the total area of cross-section. This means that D/D_a is equal to ε. This relationship was adequate to obtain the diffusion through highly porous textile structures, but for less-porous textile materials the amount of diffusion occurring is much less than that obtained in this manner.

If one considers the case of diffusion through a highly porous bed made up with solid spheres and compares it with the analogous case of conduction, the picture is that of conduction through a continuum of good conductor with spheres of insulator interspersed in the good conductor. Maxwell[2] gave the following equation for these conditions:

$$k = k_s \frac{1 - \left(1 - a\frac{k_s}{k_p}\right) b}{1 + (a-1)\,b}$$

where $$a = \frac{3k_s}{2k_s + k_p}, \quad b = \frac{v_p}{v_s + v_p}$$

where k_s is the conductivity of the solid—the good electrical conductor; k_p is the conductivity of the pores—the spherical air spaces in the good conductor; v_p and v_s are the relative volumes of pore and solid.

For the case of diffusion the suffixes must be interchanged, that is, the interspersed spheres are the solid—thus $b = (1-\varepsilon)$. Assuming the diffusion through the solid is zero, this leads to $D/D_a = 2\varepsilon/3-\varepsilon$. In Fig. 1 experimental data due to Penman[3] for particulate systems are plotted, and it can be seen that curve B based on Maxwell's equation gives the general shape of the curve followed by the experimental points. Penman suggested that $\frac{D}{D_a} = \frac{2}{3}\varepsilon$, and it can be seen that, when ε is small, the above expression tends to this value. Maxwell's equation applies strictly only for high porosities, but it nevertheless shows good agreement with points from experiments using beds of glass spheres and beds of sand where the porosity is quite low. The line $D/D_a = \varepsilon$ has been drawn on Fig. 1 and gives a first approximation to the results.

If one considers diffusion through the gap between two parallel solid cylinders, values of D/D_a may be calculated for various spacings of the cylinders. A relaxation method has been used to compute such values. When the cylinders are interwoven by other cylinders perpendicular to them the porosity can be

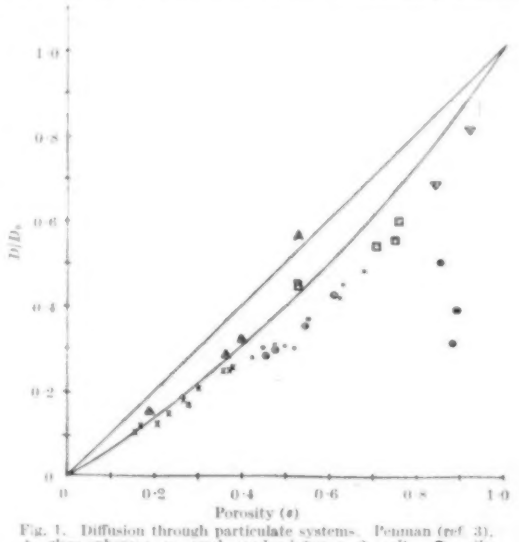

Fig. 1. Diffusion through particulate systems. Penman (ref. 3). △, glass spheres; ×, sand, sand mixture; ○, salt; ●, soil; □, talc; ▽, kieselguhr; ⊗, mica. *A*, $D/D_a = \varepsilon$; *B*, $D/D_a = 2\varepsilon/3-\varepsilon$

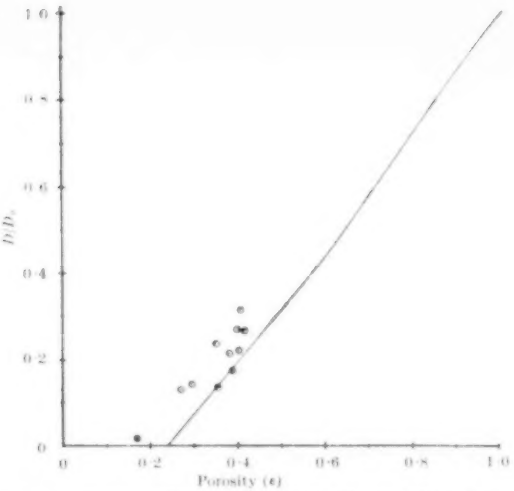

Fig. 2. Diffusion through leather. Robinson and Topp (ref. 5). ○, experimental; —, theory

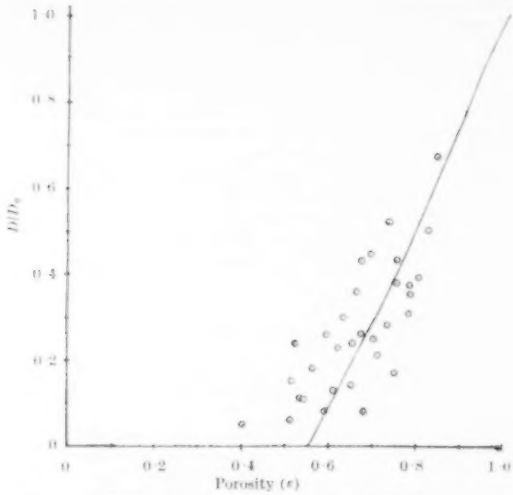

Fig. 3. Diffusion through textiles. Fourt and Harris (ref. 6). ○, experimental; —, theory

calculated as shown by Pierce[4], who considered such a geometrical configuration in connexion with textiles. In Fig. 2 the curve relating D/D_0 and the porosity obtained in this manner is given. Some experimental data due to Robinson and Topp[5] for the diffusion of water vapour through leather are compared with the curve, and it can be seen that there is reasonable agreement. The collagen fibres in leather are interwoven so that the model used is a suitable one. When the parallel cylinders touch, diffusion is no longer possible but there is still a value of porosity. Thus the curve has an intercept on the porosity axis and differs in this respect from the curve for spheres (Fig. 1)—when the spheres touch there is still a path around them for diffusion. In a woven structure the parallel cylinders cannot touch along their entire length and thus there will always be some diffusion. This is probably the reason why the experimental points for leather are to the left of the curve.

So far as textiles are concerned the model fits the case of the woven yarns. The fibres in the yarns are twisted together so that a direct path through a yarn via gaps between fibres is unlikely. If one assumes that there is no diffusion through the yarns and applies the case of the parallel cylinders to the yarns only, then the curve given in Fig. 3 results. The values have been obtained using the average porosity of yarns found by Pierce to apply to all cotton yarns in woven fabrics. Experimental data for textiles due to Fourt and Harris[6] is compared with the curve and it can be seen that there is again reasonable agreement.

It has thus been possible to obtain values for diffusion through porous materials from theoretical considerations even in the case of textile structures. These latter have often given anomalous results when suggested equations for permeability have been applied to them.

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GENETIC POLYMORPHISMS IN THE EGG ALBUMEN PROTEINS OF THE DOMESTIC FOWL

By I. E. LUSH
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RECENTLY, Sibley and Johnsgard[1], using paper electrophoresis, indicated that they had observed differences in the protein 'profiles' of egg albumen between hens of several breeds. With starch gel[2] it has been possible to establish the existence of consistent differences between the electrophoretic patterns of the albumen proteins of individual hens from sixteen small closed populations. It has further been found possible to classify these differences and to accumulate sufficient genetic results for a tentative explanation of their inheritance.

The thin albumen from eggs which had been kept up to four weeks at 4° C. was drained into muslin-covered beakers and then used for electrophoresis without any treatment, absorbed on to filter paper inserts. The storage had no effect on the electrophoretic analysis. The discontinuous buffer system of Poulik[3] was used, slightly modified (gel: 0·076 *M tris*, 0·005 *M* citric acid; *p*H 8·65. Electrode vessels: 0·3 *M* boric acid, 0·1 *M* sodium hydroxide *p*H 8·81). Gels were stained overnight with 0·005 per cent nigrosine or with 1 per cent naphthalene black 12*B* for 15–30 min., and photographed by transmitted light. Nigrosine reveals the pre-albumins better than does naphthalene black.

Eggs from the sixteen closed populations listed in Table 1 were investigated. All except the Bush Cross-

bred population have been subjected to some degree of selection or inbreeding, or both. The Bush Crossbred population is the F_2 generation of a 4-way cross involving commercial birds of four breeds; White Leghorn, Rhode Island Red, Indian Game and Light Sussex. The Jungle Fowl have been maintained as a small flock of 12–15 birds for about eight years at the Ministry of Agriculture Veterinary Laboratory, Lasswade. The Wicob White Leghorns are a flock of very heterogeneous origin kept at the School of Agriculture, Cambridge. The brown Leghorn, *Q* and Bush Crossbred are fed on Poultry Research Centre (P.R.C.) breeder mash[4], and the others on comparable standardized diets.

The Albumen Phenotypes

Considering the electrophoretogram as a whole, all but one of the 470 hens tested during a period of six months lay eggs that fall into one or other of nine distinct albumen phenotypes. 67 hens have been tested twice and 6 hens six times or more, and all except one hen described below have been consistent in their egg albumen phenotype. The albumen types differ in one or more of three separate regions of the electrophoretogram, designated I, II and III. Fig. 1 is a starch-gel electrophoretogram, which has been stained with naphthalene black, of albumen from five different eggs which between them show all the elements of variation that have been found. Sample 1 is from the Large Egg population, samples 2 and 3 from Red Plumage, sample 4 from Breeding, and sample 5 from Bush Crossbred. The wide range of intensities of the stained fractions makes photography unsatisfactory and a clarifying diagram has been added.

The two pre-albumins visible with nigrosine staining are marked in Fig. 1. One is barely separated from the main ovalbumin complex and the other lies along the brown buffer boundary referred to by Poulik[3].

Region I. Ovalbumin has been shown to consist of three components differing in phosphorous content[3]. The question of whether the variation to be described in region I of the gel involves ovalbumin itself or one or more closely adjacent proteins is left open by the use of the purposely non-committal symbol I. The same argument applies to the other regions in which the pattern varies, in both of which the particular protein involved is unknown. Region I presents two alternative variants. In I.*A*, fractions 6 and 7 are present and fraction 5 cannot be detected. In I.*b*, fractions 6 and 7 are absent, fraction 5 clearly present and the main ovalbumin complex of fractions 3 and 4 travels slightly faster than in I.*A*, although this last effect is sometimes obscured by distortion of the

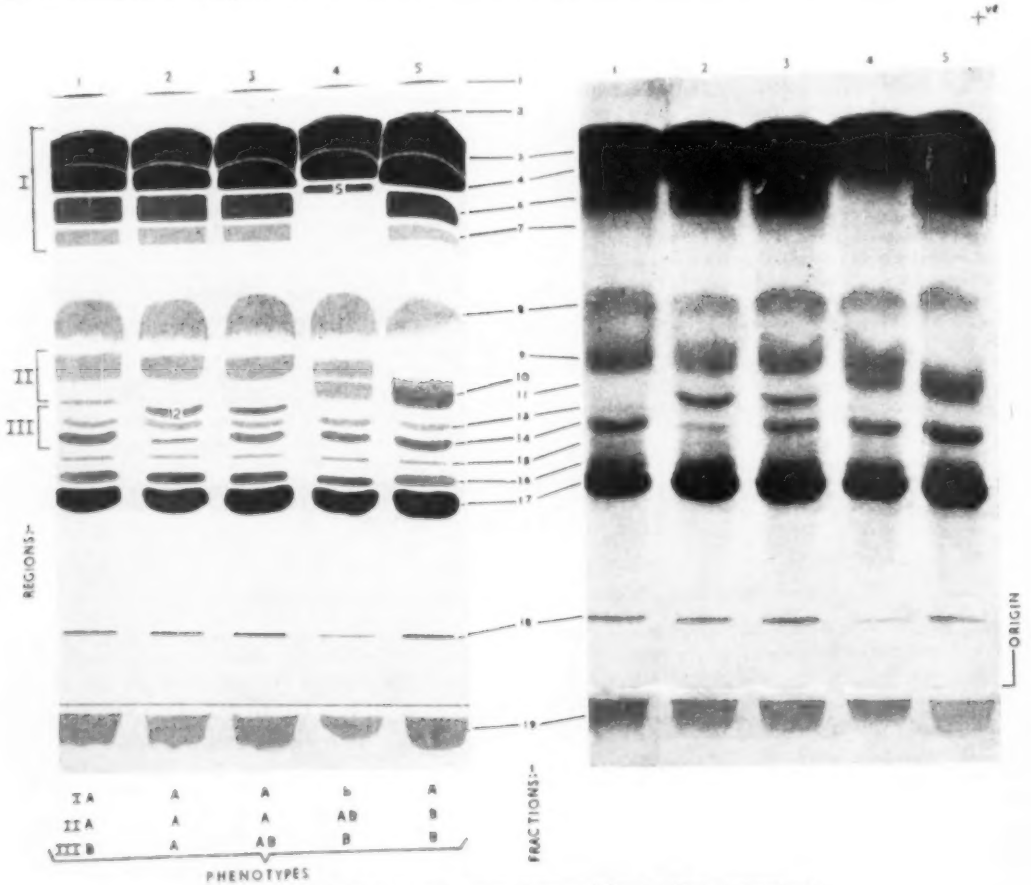

Fig. 1. Starch-gel electrophoretogram of representative egg albumen phenotypes

Table 1. Distribution of Egg Albumen Variants in Present Generation of Hens from 16 Closed Populations

Population	Regions of electrophoretogram									Co-efficient of in-breeding (per cent) *F*
	I Variants		II Variants			III Variants				
	A	*b*	*A*	*AB*	*B*	*A*	*AB*	*B*		
Brown Leghorn P.R.C. selected lines										
1. Breeding *B.*	19	56	53	22				75		31*
2. Large egg *L.*	34		34					34		64*
3. Intensity *I.*	38	4	42					42		46*
4. White plumage *W.*	10	4	14					14		62*
5. Red plumage *R.*	38		38			23	15	(3)†		74*
6. Non-moult *N.*	27		27				1	26		57*
7. Small egg *S.*	7		7			6	1			79‡
8. Dwarf body *D.*	13		13				7	6		58†
White Leghorn Reaseheath in-bred lines										
1. *RE*	25		25			25				98·63
2. *CH*	18		18					18		99·62
3. *IA*	20		20					20		99·57
4. *WA* (cuckoo Leghorn) Cambridge Wicob	12		12					12		99·11
	22		22				3	19		—
Rhode Island Red Q Inbred line	9		1	3	5		2	7		92·55
Bush crossbred	12		5	4	3		1	11		—
Jungle fowl	2		1	1				2		—

* Coefficient of inbreeding computed up to 1958.
† Surviving members of a previous generation.
‡ Coefficient of inbreeding computed up to 1953.

electrophoretogram. In Fig. 1, sample 4 is I.*b* and the rest are I.*A*.

Region II. Three variants have been found, involving fractions 9 and 10. In II.*A*, fraction 9 is present and fraction 10 is absent, in II.*AB* both fractions are present, and in II.*B*, fraction 9 is absent and fraction 10 present. In Fig. 1, sample 5 is II.*B*, sample 3 is II.*AB* and the rest are II.*A*. The diffuseness of fractions 9 and 10 makes it difficult to judge their intensity of staining by eye, but within a population that contains all three variants both fractions seem more strongly stained when they occur alone than when they occur together.

Region III. This also shows three variants. In III.*A*, fraction 12 is strongly present and fraction 14 is faint. In III.*AB* both are fairly strong, with 14 usually slightly stronger than 12. In III.*B*, fraction 12 is absent and 14 strongly present. In Fig. 1, sample 2 is III.*A*, sample 3 is III.*Ab* and the rest are III.*B*.

Several of the protein fractions have a very distinctive shape and character. Fraction 11, which tends to be obscured by 10 and 12, is rather variable in position but usually runs just ahead of fraction 12 and never behind it. The amount of some of the fractions, as judged by staining intensity, appears to be subject to quantitative genetic variation between populations, subsidiary to the phenotypes described above. For example, in Intensity and Bush Crossbred eggs, fractions 9 and 10 are typically stronger than in eggs from elsewhere, and in the Bush Crossbred eggs fraction 14 was also unusually strong (Fig. 1, sample 5). Within the Breeding line fraction 18 is weaker in some individuals than in others (Fig. 1, sample 4). Wilcox and Cole[4] found that the lysozyme concentration in egg albumen is amenable to selection both up and down, so quantitative differences are to be expected. The age of the hen and the position of the egg in the clutch seem to be without effect on the albumen phenotype. The first three eggs of one Large Egg × Breeding F_1 pullet gave a typical I.*A*, II.*A*, III.*B* pattern.

The distribution of the regional variants in the current generation of hens from sixteen closed populations is listed in Table 1. Of the nine phenotypes found so far, five can be read directly from Table 1 in those populations that vary only in one region, two others are recorded in Table 3 and the remaining two (I.*A*, II.*AB*, III.*AB* and I.*A*, II.*B*, III.*B*) were both present in the Bush Crossbred and Q populations.

Genetical Data

The genetical data suggest that the variation at the three regions is caused by segregation at three corresponding loci, two alleles segregating at each locus.

In region I the hypothesis of two alleles at a sex-linked locus was at first suggested to explain the two variants, but it had to be abandoned in the face of the pedigree from the Intensity line summarized in Table 2. If the locus is sex-linked, then in order to produce offspring both I.*A* and I.*b* the sire (being the homogametic sex) must be heterozygous, and the two variants should be present in approximately equal numbers. On this hypothesis the observed distribution would be very improbable ($\chi^2 = 9{\cdot}39$, $P < 0{\cdot}005$). Unfortunately, the dams of the two I.*b* offspring died too soon to be tested, but the argument is still valid. Several I.*A* and I.*b* dams have produced daughters of both types. Therefore locus I cannot be borne on a *W* chromosome.

Table 2. Egg Albumen Phenotypes in a Half-family from the Brown Leghorn Intensity Line

Sire	Phenotypes of dams	Phenotypes of offspring	
		I.*A*	I.*b*
Cock. *G.* 3839	(dead)	3	
	I.*A*	5	
	I.*A*	4	
	(dead)	1	1
	(dead)	3	1

Since only two variants have been seen in region I, an autosomal locus with one allele dominant over the other must be postulated. It will be shown here that the allele determining the I.*A* variant is dominant over the allele determining the I.*b* variant, and it is proposed that the dominant allele be symbolized by I^A and the recessive allele by I^b. The heterozygote, I^A/I^b, hen would then lay eggs of type I.*A*.

F_1 hybrids between several of the Poultry Research Centre selected lines have been produced in the course of a programme of work on heterosis in this laboratory. Of these, 34 F_1 hens from the following crosses have been tested: Breeding × Large Egg, and its reciprocal; Breeding × Red Plumage, and its reciprocal. All 34 hens laid eggs with I.*A* albumen. If I^A is dominant over I^b, then I^b can only be present in the Red Plumage and Large Egg lines in heterozygotes, in the cocks, or in the untested hens (less than 5 in either line), and I^A must be the more frequent allele in these two populations. It would then be expected that most of, or even all, the hybrids with Breeding would be phenotypically I.*A*, which they are. If I^b is dominant over I^A, then the absence of I.*b* hens among the hybrids is inexplicable. 8 of the hybrids came from Breeding dams known to be I.*b*. If I^b is dominant, these dams must be heterozygotes and their progeny should approximate to a 1 I.*A* : 1 I.*b* ratio. The

Table 3. Distribution of Egg Albumen Phenotypes in the Brown Leghorn Breeding Population

Pooled data from the current generation and the surviving members of the three previous generations

Variants	Variants II.*A*	II.*AB*	II.*B*	Totals
I.*A*	26	5	0	31
I.*b*	48	27	2	77
Totals	74	32	2	108

observed absence of I.*b* hens among the 8 hybrids makes this hypothesis untenable ($\chi^2 = 6{\cdot}12$, $P < 0{\cdot}02$).

In region II, fractions 9 and 10 can be considered separately or together. If separately, it can be postulated that the presence and absence of fraction 9 are determined by two alleles at one locus, one allele being dominant over the other. Fraction 10 could be determined in the same way at a different locus. If together, it can be postulated that each of the two protein fractions is the product of a different one of two alternative alleles at only one locus, locus II; in other words, a one gene equals one fraction (= one protein) relationship. The available data are compatible with any of these hypotheses, but the last seems most acceptable for the following reasons. No egg albumen which lacks both fractions 9 and 10 has been found. Fractions 9 and 10 resemble each other in shape and diffuseness, and differ in these respects from most of the others. Finally, as was mentioned before, when both fractions are present there seems to be less of them than when they are present separately, so long as the comparison is made within a population. If the single-locus hypothesis is confirmed, the alleles determining the presence of fractions 9 and 10 may be symbolized by *IIA* and *IIB* respectively.

Table 3 shows the distribution of phenotypes in the Breeding line, both the present generation and the surviving members of the three previous generations. There is a slight but not significant association between I.*A* and *IIA* ($\chi^2 = 5{\cdot}01$, $P > 0{\cdot}05$). In both the present and the pooled Breeding line data the distribution of the region II variants does not differ significantly from a Hardy-Weinberg distribution.

In region III the genetical data and the electrophoretic variation resemble region II and the same arguments apply, with one complication. Let us postulate a locus III at which two alleles, *IIIA* and *IIIB*, determine the presence of proteins 12 and 14 respectively. In the homozygote *IIIB*/*IIIB*, only protein 14 is synthesized, in the heterozygote *IIIA*/*IIIB* both proteins are present, and in the other homozygote *IIIA*/*IIIA* only protein 12 should be present, yet in fact in variant III.*A* protein 14 seems to persist (see Fig. 1). However, there is no reason for supposing that the electrophoretic separation is perfect, and the anomaly would be explained if fraction 14 were shown to be a mixture of two genetically unrelated but electrophoretically superimposed proteins, the major one subject to the genetic variation, and the minor one constantly present in every egg throughout the population. This would also explain why in the heterozygote *IIIA*/*IIIB* (giving variant III.*AB*), when both proteins might be expected to be present in equal strength, fraction 14 nearly always appears stronger than fraction 12.

If, and when, chemical identities are given to the proteins involved in the variations described, loci I, II and III can be replaced by more informative symbols. Fractions 3 and 4 are almost certainly ovalbumin[7]. Unpublished work, in collaboration with Dr. W. N. M. Ramsay, of the Department of Biochemistry, University of Edinburgh, using iron-59, has shown that small amounts of added iron are bound almost exclusively by fractions 17, 16 and possibly 15, which can therefore be included in the term conalbumin. Fraction 19 is lysozyme.

It has been mentioned that one hen was not consistent in its egg albumen phenotype. This bird, *F* 3230 from the Poultry Research Centre Intensity line, hatched in June 1957, was used between April 25 and June 14, 1960, in a control experiment to test the effect of egg storage on albumen phenotype. All 12 of the eggs used were I.*B*, II.*A*, III.*B*, and it was noticed that the lysozyme fraction was unusually variable in amount. Between August 30 and October 6 the hen laid 8 eggs, and in all but the second of these fraction 12 was present but usually less strongly than in a typical III.*AB* variant. In the last two eggs, lysozyme had almost vanished and ovalbumin was becoming progressively weaker.

Nothing resembling this has been seen in any of the other several hundred eggs examined in this work, all of which have been readily classifiable without the slightest hesitation into one or other of the phenotypes described. The anomalous changes may be caused by a pathological condition in the oviduct.

This work was done during the tenure of a British Egg Marketing Board studentship. I am grateful to Dr. A. W. Greenwood for providing facilities and to Drs. J. H. Sang, D. J. Bell and J. S. S. Blyth for helpful discussions and advice. The Jungle Fowl eggs were kindly given by Dr. J. E. Wilson.

(*Note added in proof*. The above results were obtained with freshly made starch gels. With gels which have been stored overnight at room temperature, it has been found possible to discriminate between the albumens of hens of genotypes *IA*/*IA* and *IA*/*Ib*. These findings will be described in detail elsewhere.)

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REPRODUCTION IN THE GREAT GREY KANGAROO

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TWO female great grey kangaroos (*Macropus major* Shaw) collected at Padthaway, south-east South Australia, in late October 1959, had a new corpus luteum in one or other ovary. At least one of these had recently mated, as spermatozoa were seen in glands of the sectioned uterus. In the same area females were pregnant, or had early pouch young, in late December 1959. At Blanche Town, South

Australia, females were pregnant in early November 1958. On Kangaroo Island, South Australia, the insular form of the great grey kangaroo (*M. major fuliginosus* Gould) was observed mating in late December 1956. At Padthaway, in October and December 1959, breeding females were suckling advanced young which had left the pouch, and in March and April 1960, females with hairless pouch young were suckling an older young out of the pouch. A single female, collected on Kangaroo Island in February 1958, had a hairless pouch young and a large young at heel which was being suckled. Three females in captivity at National Park near Adelaide, South Australia, were examined. In early November 1960, two were suckling young at heel and one of these had an early pouch young. The other gave birth to a young later the same month. The third National Park female had an early pouch young and was suckling a young at heel in mid December. In April 1958, at Blanche Town, and in August 1960, at Padthaway, females had large pouch young, but were not suckling young at heel.

The gestation period of the great grey kangaroo is 38–39 days[1]. The ages of pouch young, collected with their mothers in the wild, were unknown, but approximate ages were assigned by comparing them with young of known ages of the red kangaroo (*Macropus rufus* Desm.). New-born young of the two species are approximately the same weight (about 0·9 gm.) and the adults are approximately equal in size. It was assumed that growth-rates are comparable in the two species. All 11 Padthaway young examined were conceived between early October and early January and the three National Park young in early September and early and late October. The two Blanche Town young and the single Kangaroo Island young were conceived in November.

The observations on post-œstrous and pregnant females and on pouch-young indicate a breeding season from early September to early January. The great grey kangaroo breeds in December in northern New South Wales[2]. The association between mother and offspring is particularly long: suckling, in and out of the pouch, lasts at least 14 months in the Padthaway area.

Corpora lutea of pregnancy were reduced in size in March, two months after the end of the breeding season, and absent in August. However, three females taken in the breeding season had two corpora lutea of different ages. This indicates that the great grey kangaroo is polyœstrous, but I have so far been unable to determine the length of the œstrous cycle by taking daily vaginal smears of captive females.

Sharman[3] stated that lactation-controlled delayed implantation was a feature of reproduction in two species of macropod marsupials and probably occurred in at least three others. It is now known to occur also in the macropods *Protemnodon irma*[4], *Thylogale thetis*[5], *Macropus robustus*[6], *Lagostrophus fasciatus* and *Bettongia lesueur*[7]. In those species having delayed implantation that have been thoroughly investigated the gestation period is shorter than, but nearly equal to, the length of one œstrous cycle. During the period at which a quiescent, unimplanted blastocyst occurs in the uterus there is a small corpus luteum, formed at a post-partum ovulation and called the corpus luteum of lactation, in one ovary. Growth of the corpus luteum of lactation and development of the blastocyst occurs following premature loss, or removal of, the young from the pouch[3]. Female great grey kangaroos carrying young in the pouch did not have corpora lutea of lactation, and a female from which the young was experimentally removed, and which was known to have been with males at parturition, did not produce another young.

Females taken early in the breeding season at Padthaway and Blanche Town had new, developing corpora lutea in the ovaries and the uteri were in the proliferative phase. One of these, which had evidently recently mated, had the anterior vaginal canals and median vaginal culs-de-sac enlarged and filled with a creamy substance containing abundant sperm. In the others the occurrence of earlier mating could only be verified from the presence of sperms in the uterine glands. Similar conditions occur after œstrus and mating in other species of macropod marsupials[3]. Two females in late pregnancy, with embryos 19·3 and 22·0 mm. greatest length, had enormously distended anterior vaginal canals filled with creamy substance containing abundant sperm. The canals were less distended in a female with a new-born young (greatest length 21·5 mm.). No sperms were found in the vaginal canals of this female, but they occurred in the uterine glands. Copulation had thus recently occurred in these three females, but none had Graafian follicles containing mature eggs and none had recently ovulated. Mitotic activity was seen in the uterus of the female with the 22·0 mm. embryo but was not seen in the uteri of the two other females. The seminal fluid was evidently not left in the reproductive tracts from earlier inseminations because it was absent from females with earlier embryos measuring 9·5 and 19·0 mm. A little seminal fluid but no sperm was found in an animal with a 5·5 mm. embryo. No seminal fluid was found in the tract of one female with an embryo measuring 23·5 mm. greatest length.

It was concluded from these observations that delayed implantation is not a normal feature of reproduction in the great grey kangaroo as it is in related macropod marsupials. The œstrus which occurs near the end of pregnancy may be the result of possible high levels of extra-ovarian hormones secreted during pregnancy. As it is not accompanied by ovulation, it cannot be followed by fertilization as is the post-partum œstrus in related species. The possibility that this sterile copulation is the equivalent of post partum copulation in other species and that in the great grey kangaroo the gestation period has been extended beyond the limits of the œstrous cycle will be investigated next breeding season.

This investigation is based on a total of twenty-six adult females. Funds for the project came from Commonwealth of Australia Research Grants to Universities and from a generous grant from the Nuffield Foundation. The work was supervised by Mr. G. B. Sharman, who provided some of the specimens, with information on their history.

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ANALYSIS OF THE CROSS-REACTION BETWEEN TWO STRAINS OF TOBACCO MOSAIC VIRUS

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DIFFERENT virus strains are considered to be related antigenically if an antiserum prepared against each strain reacts in some way with the others. This combination, which is known as a cross-reaction, serves as the foundation for all strain relationship studies.

Although there is usually little or no controversy with the serological findings themselves, the symbolic representation of the results often do lead to dispute. This is understandable when one considers that cross-reactions may imply either of the following interpretations: (1) Each virus strain may be a mosaic possessing a number of distinct antigenic components. One or more of these components may be shared with other strains. Thus, a fraction of the antigenic surface may be identical on all strains displaying cross-reactivity, while the remaining antigenic components may be unique, and specific for particular strains. (2) Each virus strain may possess but a single kind of determinant which, however, is structurally similar to that found on related virus particles. In this case, strains are related if the spatial configurations of their surface antigens are similar to each other. They need not be identical to those found on related strains. These two cases are known respectively as the mosaic and single determinant case. They may, of course, be combined, that is, some sites may be identical on two strains while others may only be related. For our initial consideration here, however, the two cases will be treated as alternative extremes.

Frequently, in cross-reaction studies, it is not clear which of these alternatives the author has in mind, even though it is common for one or the other to be chosen almost arbitrarily. This is a problem which has been faced time and time again, and has been discussed at length by many investigators. For this reason, no attempt will be made in this article to review the subject of cross-reaction. The reader is referred instead to such general sources of information as Landsteiner[1], Kabat and Mayer[2], Race and Sanger[3], Burnet and Stanley[4], Matthews[5] and to an excellent summary of the problem from the immuno-geneticist's point of view by Owen[6]. The purpose of this article is to present a method of analysis which promises some success in distinguishing between the alternatives.

To a large extent, the difficulties encountered can be attributed to the reagents used for measurements, that is, the antisera. Both the mosaic and single determinant scheme require that the antisera which are produced, following immunization with single virus strains, are heterogeneous. The nature of this heterogeneity, however, is different for each case, so that two classes of antibody heterogeneity need to be considered.

In the first class, applicable to the mosaic case, discrete populations of antibodies are elicited, each of which combines specifically with the particular inciting antigen, and not with any of the others. These antisera are mixtures containing, at most, as many different kinds of antibodies as there are unique surface antigens on the virus used in the inoculum. Cross-reaction occurs when one of these discrete populations of antibodies combines with the surface of a related strain possessing an antigen identical to that of the immunizing strain.

In the second class, a single population of antibodies is present in each antiserum. These populations, although stimulated in response to single antigenic determinants, contain antibody molecules with broadened combining powers, capable of reacting with antigens that are structurally similar to the homologous one. The two antigenic cases and their accompanying antibody classes are summarized in Table 1.

Table 1. Possible Relationships Between Two Virus Strains Showing Cross-Reaction

Case	Strain	Antigenic surface	Antibodies
1. Mosaic	1	*A* *B*	*a*, *b*
	2	*A* *C*	*a*, *c*
2. Single determinant	1	*A*	*a*
	2	*A*¹	*a*¹

This is the simplest example in which only two strains are analysed. Theoretically, for each new virus strain studied an additional antigen and corresponding antibody could be added under the mosaic concept whereas another antigen, again similar to *A* or *A*¹ would be assumed in the single determinant case.

For simplicity, the mosaic and the single determinant cases are described separately, although they need not be mutually exclusive. The two may well be represented in any one virus as already mentioned. In addition, the number of different antigenic determinants shown is the absolute minimum. Many more may be required to characterize a particular virus, depending on the complexity of the data and the number of different virus strains examined.

Although for practical purposes of virus identification and classification, it may be of little consequence to discriminate between the mosaic and single determinant scheme, the differences are nevertheless important. Each scheme leads to a distinct view both of the physico-chemical structure of the virus surface and of the amount of genic information required for the transmission of these characteristics. Thus, on theoretical grounds, the differences are significant enough to warrant all efforts to distinguish between the two.

Because of the long and successful history of the mosaic concept as applied to cellular and bacterial investigations, it is not surprising that this scheme

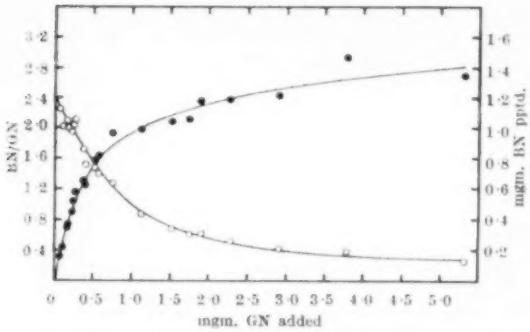

Fig. 1. Quantitative precipitin reaction. *U*2 vs. anti-*U*2 antiserum pool 17–18. Data are for antibody N precipitated in antibody excess to equivalence, and corrected to 1·0 ml. undiluted antiserum. Closed circles—antibody N (BN) precipitated. Open circles—ratio of antibody N to antigen N (BN/GN)

has played the dominant part in virus classification. On the other hand, scheme 2, that of the single determinant, deserves more serious consideration, particularly because it has been demonstrated that a variety of immunological systems conform to the single determinant hypothesis. This by no means suggests that the mosaic hypothesis as applied to virus classification is inapplicable. It does, however, suggest that one observes some restraint in assigning a series of code letters to a virus strain in order to indicate its antigenic similarities or differences with related strains without the requisite evidence.

In those cases where the reactive sites are chemically defined the required evidence can be obtained, and proper relationships established, from a qualitative analysis of cross-absorption data. Many classical examples of such analyses are given by Landsteiner[1]. Unfortunately, the chemical nature of the antigenic determinants on the surface of virus particles are as yet undefined, and qualitative cross-absorption studies on a system with chemically unknown antigenic determinants are incapable of distinguishing between the two cases. Nevertheless, a quantitative analysis of the cross-reaction curves may resolve the issue. As a case in point, the quantitative data obtained from the cross-reaction between two related strains of tobacco mosaic virus, *U*1 and *U*2, will be described.

The homologous precipitin reaction for *U*2 and rabbit anti-*U*2 is shown in Fig. 1. The reaction is characterized by a steep rise in the amount of antibody nitrogen precipitated where the concentration of antigen nitrogen added is small. This region is followed by a more gradual and prolonged increment in antibody precipitated until the equivalence zone is reached. The ratio of antibody nitrogen (BN) to antigen nitrogen (GN) combined consequently falls precipitously at first, and then less so as more antigen nitrogen is added.

The more common equations for describing the quantitative precipitin reaction are inadequate to account for these data. Although other equations can be fitted to the data, they all suffer from the same shortcoming. They assume that only a single kind of antibody is combining with one kind of antigenic configuration. In the present case, we are concerned as well with the possibility of diverse antibody molecules reacting with a number of different antigenic sites on the same virus particle. For this reason, until proved otherwise, the precipitin curve shown in Fig. 1 is assumed to be a composite of at least two reactions, the sum of which adds up to the total shown.

Before proceeding with the analysis of the precipitin curve, it is well to point out that this tobacco mosaic virus/anti-tobacco mosaic virus system appears immunologically homogeneous according to Kendall's criterion[7]. A clear equivalence zone is observed where neither antibody nor antigen (or only minute traces of each) is detected in the supernatant liquid after the precipitates have been removed by centrifugation. This implies, by definition, that all *U*2 particles are identical with respect to antigenic characters and that there are present no detectable amounts of contaminant virus or other antigenic units and corresponding antibodies different from the bulk virus and antibody population studied in the reaction. This point cannot be over-emphasized. In those cases, for example, where it is demonstrated that different antigenic determinants are carried on distinct and separable molecules, the following analysis does not apply.

The Mosaic Case

Considering the mosaic hypothesis first, a resolution of the precipitin curve into two component parts can be accomplished if the following conditions be assumed:

(1) There are two discrete kinds of antigenic sites on the virus called *A* and *B*. Each type makes up some specified fraction of the total number of combining sites.

(2) Each type of antigenic site in turn stimulates the production of an antibody population which is specific; so that anti-*A* (*a*) reacts only with *A* and anti-*B* (*b*) only with *B*.

(3) No interference is encountered during precipitation by either antibody type. The reactions of anti-*A* with *A* and anti-*B* with *B* occur independently of each other and progress to a final state which can be predicted from the concentrations of each antibody population and the two kinds of antigenic sites described in (1).

(4) In the presence of an excess of both antibodies, the maximum number of respective virus valences will be satisfied, and within this range of antibody excess the amount of antibody precipitated will conform to the quadratic equation proposed by Heidelberger and Kendall.

The observed shape of the precipitin curve imposes certain restrictions on the calculations of the fraction of antigenic sites assigned to *A* and *B* and on the concentration of the respective antibodies. With this limitation in mind the precipitin curve shown in Fig. 1 was resolved to a reasonable degree, by trial and error, into the components appearing in Figs. 2 and 3. This resolution is unique, for no other combination of two precipitin curves will satisfy the data better. From the maximum antibody-antigen ratios obtained in Fig. 3, the fractions of the total antigenic sites which are *A* and *B* are estimated. Approximately 0·83 (2 ÷ 2·4) are *A* and 0·17 (0·4 ÷ 2·4) are *B*.

In Fig. 2, it is seen that the amount of anti-*A* in combination with *A* rises steeply with small additions of virus, since most of the viral surface is *A*. With the addition of 0·55 mgm. of virus nitrogen all the anti-*A* is bound. From this point on, a constant amount of anti-*A* is found in the precipitate in addition to the increasing amounts of anti-*B*. The equation for the first part of the *A*/anti-*A* precipitin

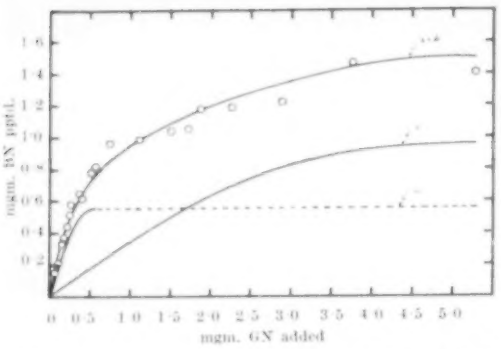

Fig. 2. Quantitative precipitin reaction. *C*2 vs. a hypothetical antiserum containing a mixture of antibodies *a* and *b*. The curves relate the amount of antibody N contributed individually by *a* and *b* to the precipitate and also the sum of the two. The open circles are the experimental points for antibody N precipitated taken from Fig. 1

curve is $BN_A = 2{\cdot}0\ GN - 1{\cdot}82\ \overline{GN}^2$, where BN = antibody nitrogen precipitated and GN = antigen nitrogen precipitated.

The combination of *B* with anti-*B* progresses over a more extensive range since relatively little of the virus surface is *B*. Therefore, much larger amounts of virus nitrogen are required to bring the *B*/anti-*B* system to equivalence. At the point of equivalence for the *B* antigen the entire complex system reaches equivalence. Beyond this, further additions of virus will lead to an antigen excess zone. The equation describing the *B* system is $BN_B = 0{\cdot}4\ GN - 0{\cdot}042\ \overline{GN}^2$, where the symbols have the same meaning as before.

The gross precipitation observed is the sum of the two quadratic equations to the point of equivalence for the *A* system, or $BN = 2{\cdot}4 - 1{\cdot}86\ \overline{GN}^2$. Beyond this point $BN_{total} = C_A + 0{\cdot}4\ GN - 0{\cdot}042\ \overline{GN}^2$, where C_A is a constant equal to the maximum anti-*A* content of the antiserum. In this case $C_A = 0{\cdot}55$ mgm.

Granted such a complex precipitating system, certain predictions can be made concerning any cross-reaction observed with this antiserum and related virus strains. The following cases are then logical consequences of the mosaic hypothesis:

Case 1. Both *A* and *B* are present on the test strain. In this case cross-absorption would remove all anti-*A* and anti-*B*. The test strain would be judged on this basis to be identical to the homologous. The test strain may not be identical in quantitative tests, if it were shown that either the ratio of *A* to *B* were different or the combined total of *A* and *B* was more or less than on the homologous strain, or that an antigen *C* was present in addition to *A* and *B*.

A quantitative analysis of the cross-precipitin curve would not detect '*C*' in these circumstances, but would reveal whether or not the total number of combining sites for anti-*A* and anti-*B* were different from that of the homologous strain.

This information would be obtained by noting any changes in the maximum antibody-antigen ratio. A value of less than 2·4 would indicate fewer identical sites on the related strain, and thereby suggest the possibility of an additional antigen not found on the homologous strain. Alternatively, such data may be interpreted as suggesting a decreased surface-to-volume ratio for the virus particle with a concomitant reduction in the total number of antibody molecules that can be attached to the surface of the virus. An antibody–antigen ratio significantly greater than 2·4 would almost certainly imply a smaller virus particle with identical surface antigens.

Case 2. *A* is present on the test strain, but *B* is not. Cross-absorption would remove approximately one-third of the antibody. The two-thirds remaining, or anti-*B*, would react with the homologous strain.

If the test strain possesses no antigenic grouping other than *A*, the antibody–antigen ratio in the cross-precipitin curve would extrapolate to 2·4. If the test strain possesses other non-related antigenic groups and the size and shape of the virus particle were identical to the homologous strain, then the extrapolated ratio would be less than 2·4, in proportion to the fraction of the total which is *A*.

The absorbed antiserum, which now contains only anti-*B*, will react with only that portion of the surface of the homologous strain which is represented by antigen *B*. Therefore, after cross-absorption the precipitin curve for the homologous reaction should always show a decrease in the maximum antibody–antigen ratio.

Furthermore, if the cross-reactive antibody (anti-*A*) is dissociated and recovered from the heterologous precipitate it, too, when treated with the homologous strain, should reveal a drop in the antibody–antigen ratio. The two ratios, the one obtained with the non-absorbed antibody plus the one obtained with the dissociated antibody, should add up to 2·4.

Case 3. *B* is present on the test strain, but not *A*. The analysis for this case is identical to Case 2.

One further consequence of a multiple system is that partial absorption of the antiserum with its homologous strain should also lead to a fractionation of the antiserum. For example, from Fig. 2 a small amount of antigen nitrogen could be added, sufficient to precipitate all of anti-*A* but only a part of anti-*B*. The remaining unprecipitated antibody would then react in a different way (revealed by a drop in BN/GN ratio) from both the whole unabsorbed antiserum and the antibody recovered from the precipitate after dissociation.

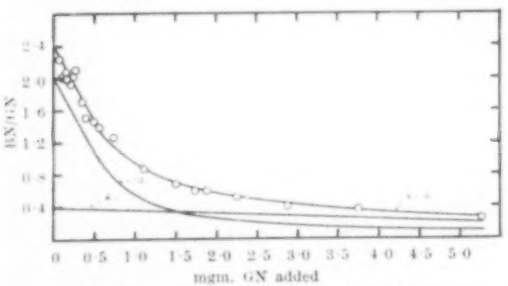

Fig. 3. Quantitative precipitin reaction. *C*2 vs. a hypothetical antiserum containing a mixture of antibodies *a* and *b*. The curves relate the ratios of antibody N to antigen N found in the precipitates individually for *a* and *b* and for the sum of the two ratios. The open circles are the calculated values taken from the experimental results shown in Fig. 1

The Single Determinant Case

Two different and detailed analyses of the tobacco mosaic virus/rabbit anti-tobacco mosaic virus precipitin curve, based on the assumption that a single population of antibodies was reacting with one kind of antigenic configuration, have been presented elsewhere[8,9] and so will not be repeated here. For purposes of the present discussion, it is sufficient to

note that under the single-determinant hypothesis, none of the preceding attempts to fractionate the antiserum into two discrete and unrelated antibody populations would be successful. Cross-precipitation with related strains would be characterized solely by a drop in titre, since only a portion of the antibody population would be expected to possess any reactivity towards the related antigen. In general, the more perfect the correspondence between the test antigen and the homologous one, the larger the antibody fraction which will react, and the greater will be the similarity in the precipitin curves. No change in the maximum antibody–antigen ratio would be expected either in the cross-reaction (provided again that the surface-to-volume ratio of the heterologous strain is the same as the homologous one), or in the homologous reaction after complete heterologous absorption. Furthermore, no fractionation again into two unrelated antibody populations would be accomplished by partial absorptions with the homologous virus.

A note of caution should be introduced at this point, since such cross-, partial-, or multiple-absorptions have been known to reveal univalent antibody[2]. When present in an antiserum, these univalent antibody molecules commonly co-precipitate with the aggregates initially formed by the divalent antibody and the multivalent antigen. Characteristically, such additions alter the shape of the precipitation curve from a simple quadratic form to one resembling the tobacco mosaic virus/anti-tobacco mosaic virus curves. Thus, the steep initial segment of the antibody curve shown in Fig. 1 may represent essentially the precipitation of divalent antibody, while the more extensive gently rising portion, on the other hand, may indicate the participation of co-precipitating univalent antibody. If this were true, then the precipitation curve observed with antibody dissociated from the homologous partial absorption would be qualitatively quite different from that observed for both the remaining unabsorbed antibody and the original antiserum. This was not observed. The general features of the precipitation curves were always the same as those seen in Fig. 1. Thus, if univalent antibodies were present, they contributed very little to the overall precipitation curve.

It is apparent from the foregoing that the most sensitive datum for distinguishing between the mosaic and single determinant case is the maximum extrapolated value for the antibody–antigen ratio in

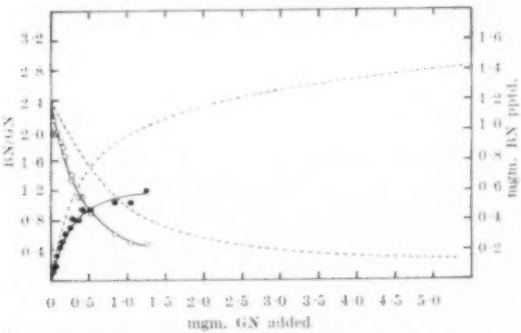

Fig. 4. Quantitative precipitin reaction. *U*1 vs. anti-*U*2 antiserum pool 17–18. Continuous lines are data for the cross-reactive virus *U*1 in antibody excess and corrected to 1·0 ml. undiluted antiserum. Closed circles—antibody N precipitated. Open circles—ratio antibody N to antigen N (BN/GN). Broken lines are the data for the homologous reaction shown in Fig. 1 drawn to the same scale for comparison

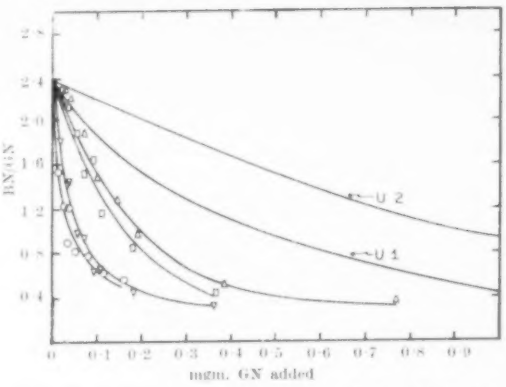

Fig. 5. Quantitative precipitation reaction. Ratios of antibody N to antigen N (BN/GN) revealed after different absorptions of anti-*U*2 antiserum pool 17–18. Lines *U*2 and *U*1 are reference lines of the homologous and heterologous reaction taken from Figs. 1 and 4 and drawn to scale. The following data are uncorrected for the different dilutions encountered: △, after complete heterologous absorption of the antiserum with *U*1 the remaining antibody was precipitated with *U*2; ▽, reaction with homologous *U*2 virus of antibody recovered after acid dissociation from *U*1 anti-*U*2 precipitate; ○, after partial absorption of antiserum with homologous virus, the remaining unabsorbed antibody was treated again with *U*2; □, the precipitate from the partial homologous absorption was dissolved in acid and antibody recovered. This antibody was reacted with *U*2

extreme antibody excess. Any difference in number, or kind of antigenic configuration, will be revealed by some change in the estimation of this maximum ratio. Such changes in ratio were looked for in the tobacco mosaic virus system under investigation, but were not detected.

Fig. 4 relates the quantitative course for the cross-precipitation of *U*1 and anti-*U*2. Apart from the obvious diminution in the quantity of antibody precipitated by the heterologous antigen, the qualitative shape of the precipitin curve is similar to that of the homologous reaction. Furthermore, the extrapolated value for the maximum antibody–antigen ratio does not appear to be different from 2·4. Thus, the antiserum reacts with as many determinant groups on *U*1 as it does on its homologous strain, *U*2.

After complete removal of the cross-reactive antibody by absorption of the *U*2 antiserum with *U*1, the remaining antibody was treated with *U*2. The precipitin curve showed no change in the maximum antibody–antigen ratio. This suggested that no fractionation of the original antiserum, of the kind proposed under the mosaic hypothesis, was accomplished by this procedure. Other attempts to reveal unique antibody populations also failed. The complete data are presented in Fig. 5.

The reciprocal cross-reactions employing an anti-*U*1 antiserum were also investigated. The data were similar to those shown in Fig. 5, suggesting again that only a single antigenic determinant was involved in these reactions. Although this interpretation of the data is the preferred one, at least one other possibility may be entertained.

Tobacco mosaic virus is known from X-ray studies and chemical analyses to be composed of approximately 2,130 protein sub-units[10]. Each of these sub-units is presumed to be antigenic. However, the maximum number of antibody molecules that can combine with an intact tobacco mosaic virus rod has been estimated[9] to be between 700 and 1,200. Thus half or more of the antigenic surface may remain uncombined, as seen in Fig. 6, even under the most

favourable conditions of antibody excess simply because of steric hindrance.

Since the experimental evidence tends to favour the notion that only one-third rather than one-half of the sub-units can be combined with antibody, the model described in Fig. 6 will be considered further. Assuming that the model is correct, it is possible to distribute two or three antigenic determinants, but no more, over the surface of the rod in such a fashion that the expected quantitative cross-absorption data would be indistinguishable from those obtained if only a single determinant were present. The different antigenic combining groups must be arranged in the precise serial order of *ABCABCABC* . . . etc., if three are present and *AABAABAAB* . . . etc., if only two are involved. These arrangements are unique. No other, or random distribution of the determinants on the sub-units would yield the same data, nor would four or more different sub-units arranged in any fashion yield comparable results. Consequently, the quantitative precipitation data are capable of distinguishing between the single determinant and the mosaic hypothesis in all cases except the two highly restrictive ones where exactly one-third or two-thirds of the sub-units are *A* and the arrangements are precisely ordered. All the combinational possibilities are described in Fig. 7.

Two general views of the precipitation of tobacco mosaic virus with rabbit antibody have now been presented. In the first and most widely accepted view of precipitation, the tacit assumption is made that in extreme antibody excess all the antigenic sites are combined with antibody. The other, as just described, is that even at best, probably no more than one-third of the antigenic sites are covered. It is under this latter view that one may entertain the notion of a mosaic antigenic structure for tobacco mosaic virus which would be extremely difficult to distinguish from one in which all of the exposed antigenic determinants were identical.

Thus, although the evidence suggesting a single antigenic determinant for tobacco mosaic virus is good, it is for the present not compelling. Positive evidence for the existence of more than one distinct exposed antigen must await a thorough serological analysis of tobacco mosaic virus sub-units of the kind prepared by Ansevin[11] and Wittmann[12]. Until

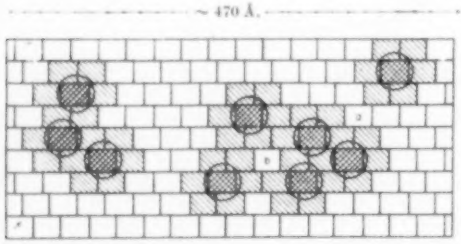

Fig. 6. A diagrammatic representation of a portion of the surface of tobacco mosaic virus showing 3 complete turns of the helix. Each rectangle represents a sub-unit 23 Å. by 29 Å. The circles represent rabbit antibody molecules (with 19 Å. short semi-axis) standing on end attached to an antigenic determinant centrally located on the cross-hatched sub-unit. The shaded areas are those that are blocked from further antibody attachments. In the upper right-hand corner, one antibody molecule exerts its influence over 6 sub-units other than the one to which it is combined. An antibody combining at *a*, will interfere with 2 sub-units not already blocked by the other antibody molecules. An antibody attaching at *b* will interfere with none that is not already blocked. This model permits a maximum combination of one-third of the sub-units with antibody molecules. (Figure taken from Rappaport, I., *J. Immunol.*, **82**, 526; 1959)

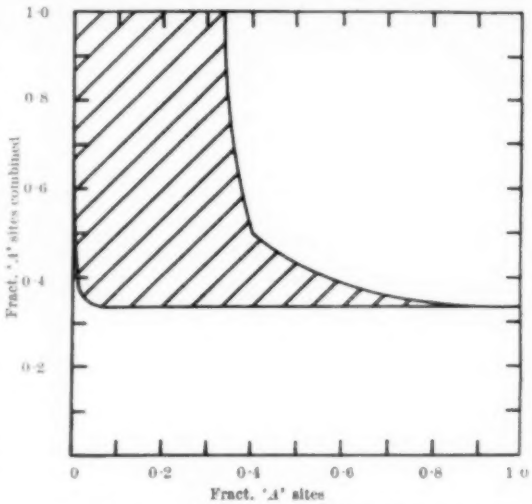

Fig. 7. The relationship between the maximum fraction of *A* sites which can be combined with antibody as a function of the fraction of sites on the tobacco mosaic virus rod which is *A*. This graph is valid for all possible sequences or arrangements of *A* sub-units making up the virus. For example, if the fraction of *A* present were 0·33 and the arrangement were ordered *ABBABBABB* . . . etc., then 100 per cent of the *A* sites could be covered with antibody molecules. If this same number of *A* sub-units were arranged side by side in a block, only 33 per cent could be combined with antibody. Any random arrangement of 0·33 *A*'s among the other antigenic sites would result in a maximum combination with antibody somewhere between 33 and 100 per cent, that is, some value in the shaded area. The shaded area, then, indicates the maximum possible combinations for all distributions of *A*

then, the single determinant scheme, with its virtue of simplicity, deserves consideration. It demands the least number of unique antigenic configurations on the viral surface, and a minimum other assumptions as well. The complex results of serological cross-absorptions are charged to the antisera employed. Antibody heterogeneity resulting from immunization with single antigens is commonplace. The problem resolves, therefore, into distinguishing between complexities that stem from an immune response and those inherent in the virus structure.

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LETTERS TO THE EDITORS

COSMOLOGY

Cosmological Significance of Angular Measurements of Distant Radio Sources

THE programme of interferometric observations of distant radio sources at present being carried out by H. P. Palmer *et al.* at Jodrell Bank may prove to be of great significance for cosmology. The preliminary results recently published[1] indicate that out of 91 sources 38 were of sufficiently small angular diameter to produce measurable interference fringes at the long base line used (32,000 λ at λ = 1·89 m.), and at least 7 had a diameter between half-power points less than 3 sec. of arc. Furthermore, these 7 were described as having "an extremely high surface brightness which is comparable with that of the intense radio source in Cygnus I.A.U. 19 *N4A*".

In the case of a steady-state universe it has been shown[2,3] that the angular diameters of sources must tend to non-zero lower limits on the observational horizon of the model ($\delta = \infty$). For a Cygnus *A* type source of colliding galaxies, Hoyle has adopted an angular diameter of 80 sec. of arc at the distance of the Cygnus source (δ = 0·056) and this leads to a horizon limit of about 4 sec. of arc. The figure 80″ is approximately the angular distance between the centres of the two radio components of the Cygnus source, so that 4″ may be taken to be the limiting half-power diameter of this source if shifted to the horizon. However, the Cygnus source has a ratio of major to minor axes approximately equal to 4, and therefore for sources of this type the average limiting diameter observed east–west would actually be nearer 2½″. It appears, therefore, that the present Jodrell Bank results are not inconsistent with the predictions for a steady-state universe.

In the case of evolutionary universes, provided we can assume that the average intrinsic distance between components of colliding galaxies does not vary significantly with epoch, predictions can be made in special cases. In the Einstein–de Sitter model the average half-power diameter of the Cygnus *A* type source specified above should not fall below a minimum value of 8½″ occurring at δ = 1·25, which is more than three times the steady-state limit of 2½″. In a Milne universe the lower limit would occur at $\delta = \infty$ and is twice the steady-state limit, that is, about 5″. In the Dirac cosmology the half-power diameter would fall to a minimum of 13″ at the relatively near point where δ = 0·73, and thereafter it would increase. Thus, all these well-known evolutionary models are placed in jeopardy by the present measurements of angular diameter.

Before applying this criterion, it is of course essential to ascertain that the sources are indeed similar to Cygnus *A*, and this can only be done for distant sources by selecting those of a surface brightness comparable to that of Cygnus *A*. According to present ideas only colliding galaxies could generate an energy flux of this high order.

In this connexion, however, attention is directed to a fact that does not appear to have been realized before, namely, that the surface brightness to be inferred for extra galactic radio sources depends strongly and explicitly on their red shift, and therefore cannot be calculated accurately from the angular diameter and apparent intensity alone, except when δ is small. Since the interpretation of any observational test in cosmology involving radio sources depends critically on what is assumed to be their luminosity function, this is evidently a matter that requires careful attention at the present time.

The formula for surface brightness may be derived as follows.

In the usual notation the general cosmological metric of homogeneous isotropic expanding world models is:

$$ds^2 = c^2dt^2 - R^2(t)\,\frac{(dr^2 + r^2d\theta^2 + r^2\sin^2\theta d\varphi^2)}{(1 + kr^2/4)^2} \qquad (1)$$

Consider a source the permanent (co-moving) spatial co-ordinates of which are (r,θ,φ). Let the surface brightness distribution function of a given element of its surface area, at the emission frequency ν and at the epoch of emission t, be $B(\nu,t)$ (W. m.$^{-2}$ (c./s.)$^{-1}$ ster.$^{-1}$). Hence the energy radiated from a surface element of proper area ΔA in the interval $t, t + dt$, in frequency-range $\nu, \nu + d\nu$, and in solid angle $d\omega$ will be:

$$B(\nu,t)d\nu dt d\omega \;\; \Delta A \qquad (2)$$

Then, if $d\omega$ corresponds to 1 sq. m. at the observer who is located at $r = 0$ at the epoch of reception t_0, we know that[4]:

$$d\omega = 1/\{R^2(t_0)r^2/(1 + kr^2/4)^2\} \qquad (3)$$

Also, if the frequency-range of reception resulting from red shift is $\nu_0, \nu_0 + d\nu_0$, and if $\Delta I(\nu_0)d\nu_0$ is the rate at which energy from ΔA in this frequency-range falls on 1 sq. m. at the observer, we may express the degradation of the energy (2) due to red shift in the form:

$$\Delta I(\nu_0)d\nu_0 dt_0 = \{B(\nu,t)d\nu dt d\omega\;\Delta A\}/(1 + \delta) \qquad (4)$$

where δ is the red shift of the source and:

$$\frac{\nu}{\nu_0} = \frac{d\nu}{d\nu_0} = \frac{R(t_0)}{R(t)} = \frac{dt_0}{dt} = 1 + \delta \qquad (5)$$

Furthermore[3]:

$$\Delta A = \frac{R^2(t)r^2\;\;\Delta\Omega}{(1 + kr^2/4)^2} \qquad (6)$$

where $\Delta\Omega$ is the solid angle subtended by the area ΔA at the observer. Whence, by (3)–(6):

$$\Delta I(\nu_0) = \frac{B(\nu,t)\;\;\Delta\Omega}{(1 + \delta)^3} \qquad (7)$$

and so the required surface brightness function is:

$$B(\nu,t) = \frac{\Delta I(\nu_0)}{\Delta\Omega}\;.\;(1 + \delta)^3 \qquad (8)$$

We note that this formula applies to either an evolutionary model or a steady-state model. In the

steady-state case $B(\nu,t)$ would be statistically independent of t, unless a selective bias depending on distance were operating in the observations.

On the other hand, the formula that appears to be generally adopted by radio astronomers has been given[5,6,7], and evidently followed in the published calculations even for very distant sources, as :

$$B(\nu_0) = \Delta I(\nu_0)/\Delta\Omega \qquad (9)$$

Since this formula is valid only for a Newtonian and non-expanding universe it may lead to serious error when applied to distant sources in the actual universe. For example, in the steady-state universe the received intensity $\Delta I(\nu_0)$ at a given frequency ν_0 must tend to zero when the source approaches the observational horizon of the model ($\delta \to \infty$). But, as I have remarked earlier, $\Delta\Omega$ tends to a non-zero limit for a given ΔA. Consequently, if in such a universe B were calculated by (9), instead of (8), it would be found to tend to zero. This is evidently a contradiction of the postulated steady state.

Another important point to notice is that $B(\nu,t)$ is calculable in this way for the emission frequency only, and in general at the epoch of emission only. Given $B(\nu,t)$, the local surface temperature would be calculable from the Rayleigh–Jeans law in the usual way, for the frequency ν and epoch t.

I have applied the formula (8) to calculate the surface brightness of the recently identified source I.A.U. 14*N*5*A*, the red shift[7,10] of which is 0·461 and the half-power diameter[4] is $4\frac{1}{2}'$. Adopting a half-power apparent intensity of 37×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$ at 159 Mc./s. for this source one finds an average temperature at the emission frequency of 232 Mc./s. equal to $1{\cdot}86 \times 10^8$ deg. K. On the other hand, the Cygnus *A* source, assuming it has a principal area of radiation of $2 \times 50'' \times 30''$ as given by Jennison and Das Gupta[8], has an average surface temperature of 7×10^7 deg. K. at 232 Mc./s. Consequently, the 14*N*5*A* source was more than $2\frac{1}{2}$ times as bright as Cygnus *A* at this frequency at their respective epochs of emission. This ratio would evidently hold over the wide range of frequencies for which the spectral indices of these two sources are nearly equal[9]. The ratio may even be as much as twice this value since we have not allowed for possible separation of components in 14*N*5*A* as we have done for the Cygnus *A* source.

It is indicated that the luminosity distribution of radio sources may be wider than has been anticipated. On the other hand, if it were found that the average brightness of the sources increased systematically with distance, assuming there was no selection effect, then this would be evidence of an evolutionary universe.

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The Interpretation of Cosmology

We are submitting herewith some further reflexions on the communication by Prof. W. H. McCrea[1], which dealt with uncertainty in cosmology.

(1) The inaccuracy of observations necessarily increases with distance. However, it cannot be excluded *a priori* that in the future the observational error concerning any chosen distant part of space could be brought below any pre-determined limit.

(2) The present cosmological theories imply a fairly large number of definite statements on future observations. This is implicitly admitted by McCrea, who points out with considerable generality that they differ from each other by $(1 + z)$, that is, by a well-determined factor[2] (z is the red shift).

It obviously follows from the above that it is a mistake to exclude the possibility of discrimination between the existing theories. (Discrimination does not mean, of course, verification.)

(3) According to McCrea, predictions relating to the immediate future of remote points of the "world picture"[3] imply an unavoidable uncertainty increasing with $(1 + z)$, that is, with the same factor by which the predictions of the existing theories differ from each other. From this he infers that the theories mentioned above cannot be distinguished from each other.

We wish to point out that in (1) the word 'prediction' is used in two different senses :

(*a*) Prediction for the immediate future of points of the world picture.

(*b*) Prediction of the results of measurements not yet carried out but considered as being realizable at an epoch, contemporary in a cosmological sense.

It is known only in theories based on an adequate cosmological principle that the two concepts are connected : in the case of these theories the immediate future of a point is definite (it is identical to the presence of a well-determined neighbouring point in the world picture). It seems to us that to go over from one meaning to the other within one and the same train of ideas may at best be justified by accepting the definite immediate future.

After these preliminaries let us examine one of the most important inferences of Prof. McCrea's communication, according to which it is in principle impossible to make a distinction between the two basic types of cosmological models. As mentioned above, if we accept our reflexion (1), we cannot deny the possibility of making a decision between the current theories. Therefore the only way to repudiate this possibility is to disprove (1) ; that is to say, to prove an irreducible uncertainty in observation. Instead of this, McCrea asserts that an irreducible uncertainty subsists as regards predictions. This, in his opinion, would characterize theories which are correct in the sense of not supposing homogeneity. It is evident that this can by no means serve as a basis for inferences regarding the distinction between existing homogeneous models. Not only is the logically relevant premise substituted by an inadequate one, but also in the same syllogism no distinction is made between the two kinds of predictions and thus McCrea's wording involves the negation of his own premise, that is, the assumption of the definite immediate future. The inaccuracy of the conclusion can be sufficiently proved by a single example : although the predictions of the Einstein universe differ from the evolutionary models only by a similar function of some distance parameter

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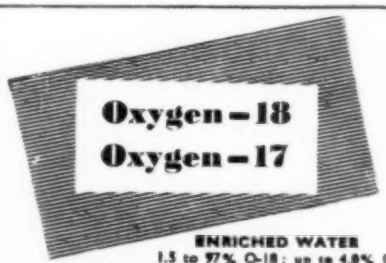

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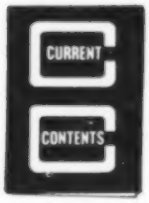

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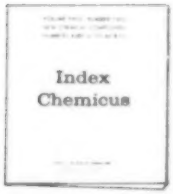

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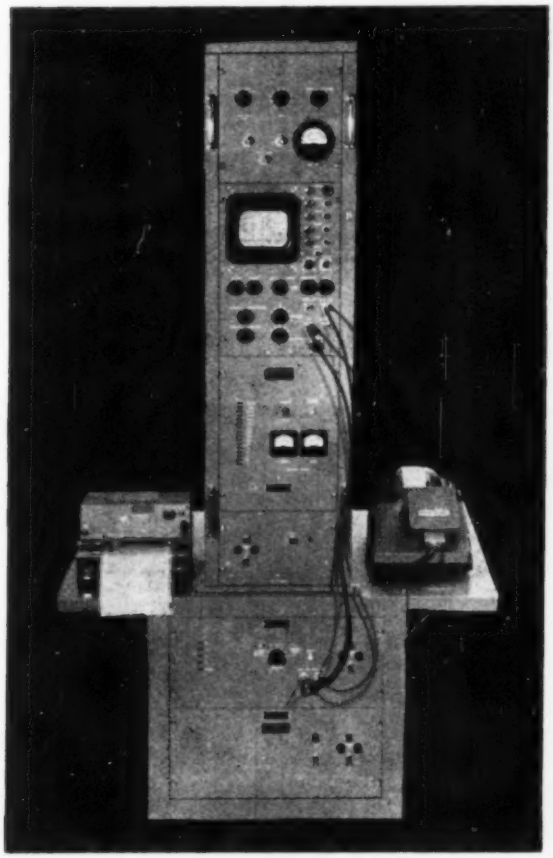

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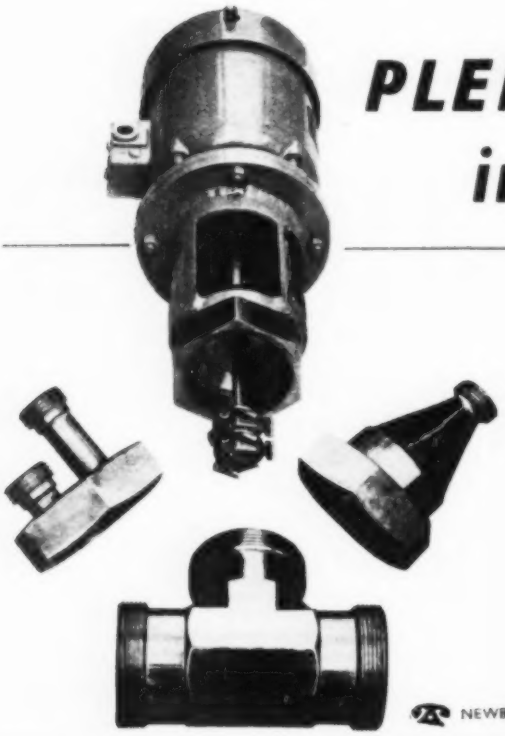

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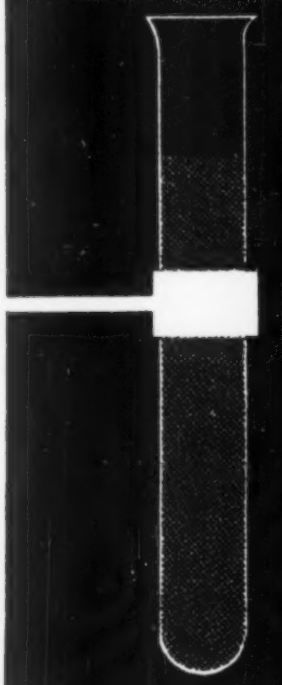

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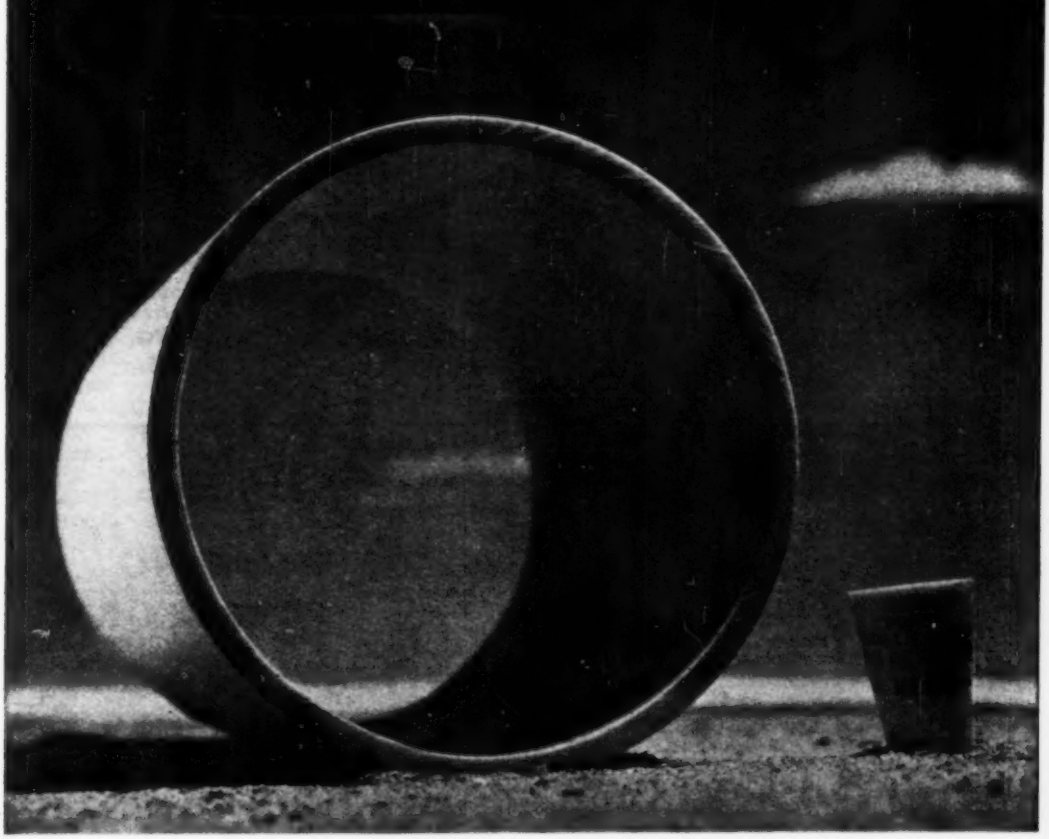

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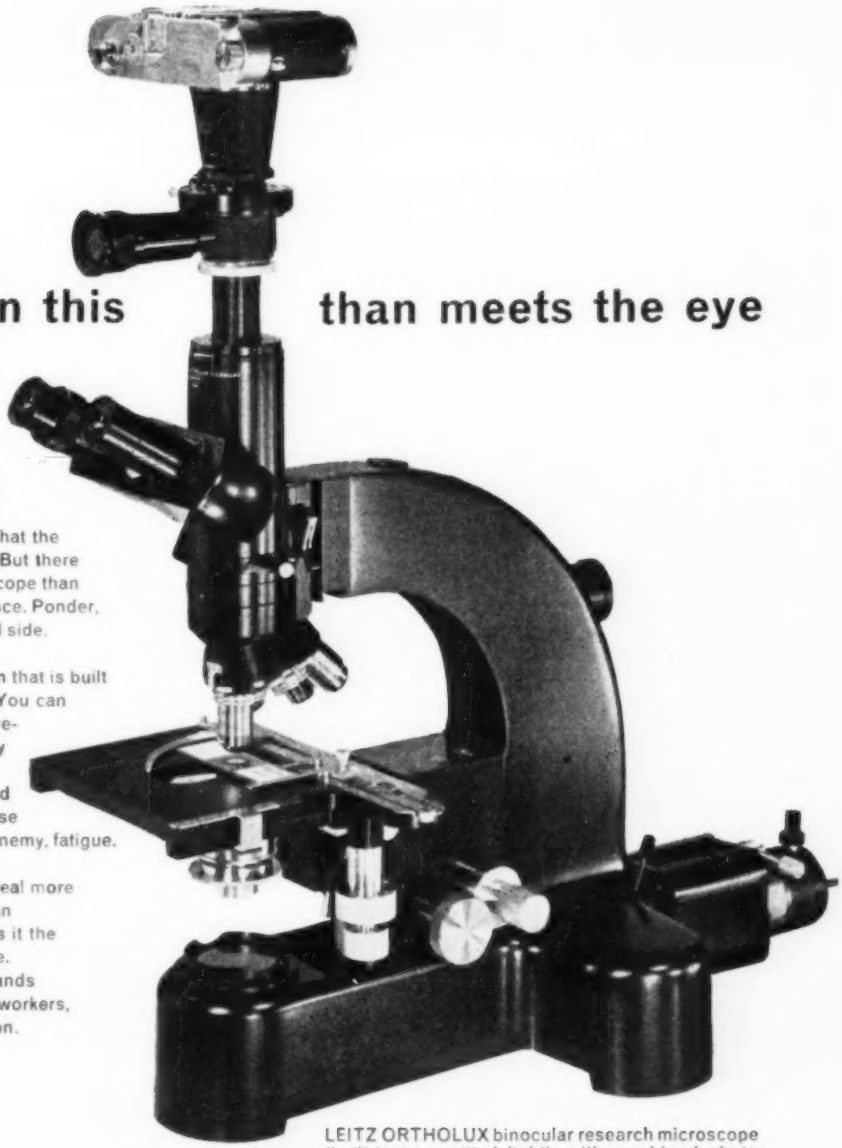

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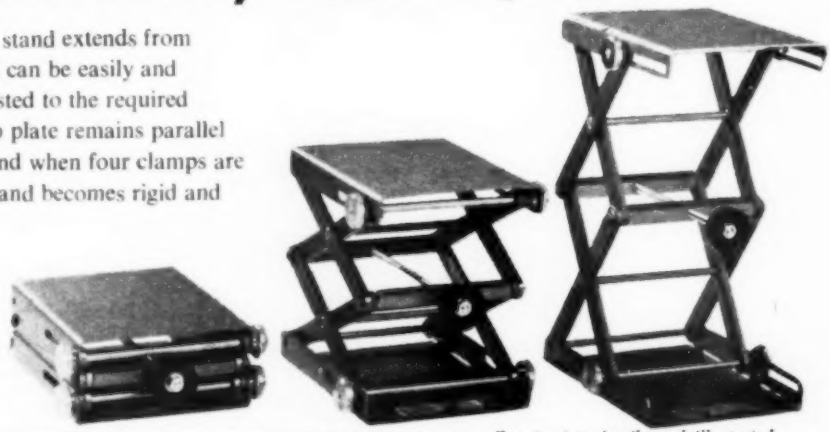

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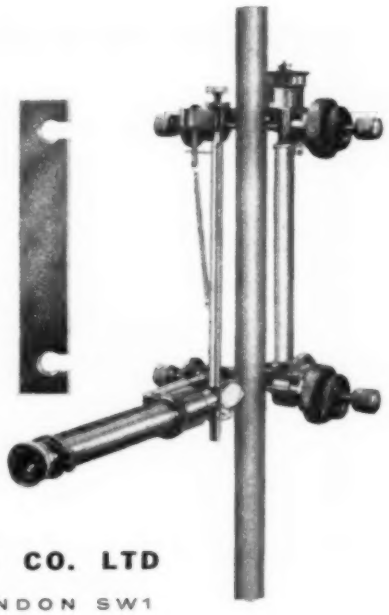

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yet observations have disproved them, beyond any doubt.

These objections in themselves do not affect McCrea's main idea, according to which, independently of the degree of theoretical development and instrumental improvement, full information on the effects influencing some remote part of the universe may be obtained only by observations continued throughout an objectively determined and cosmologically considerable period of time. McCrea infers from this that only theories embracing finite parts of space-time may be considered as realistic.

In our opinion the most valuable idea in McCrea's communication is the delimitation of what in principle is obtainable by a newly developed investigation programme. Its main deficiency is that he wants to insert the uncertainty, discovered in his own "cosmology", into the framework of well-defined theories of present cosmologies.

Neither can we accept McCrea's scientific-philosophical point of view, as we do not consider the cosmological investigations built up on working hypotheses which cannot be established directly to be superfluous. The possibility of model examinations might be understood from the following: in the first place, Nature is entitled to reject scientific prejudices (speculative considerations which are essentially subjective must be pushed into the background). Here, as in all other scientific examinations, we have to take it for granted that any inaccurate statement concerning Nature must, sooner or later, clash with an observational fact. Consequently, every logical theory built on scientific basis is justifiable, provided it is "vulnerable"[4], for example, in its predictions, so that there is the possibility for Nature to prove that it is wrong. No examples are needed to demonstrate the tremendous progress which could be made in science, through the discussion of some theories which seem, for the moment, to be controllable only in indirect ways, even if their formal aim is the examination of the universe as a whole, and the decision as to their scope is postponed for the future. Therefore we consider model investigations as one of the possible theoretical methods of cosmological examination available at the present.

B. Balázs
Gy. Paál

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Konkoly Thege Street 13–17,
Budapest, 12.

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ASTROPHYSICS

Solar Wind and the Gegenschein

To account for the motion of comet tails, Biermann[1] has suggested that there is neutral ionized hydrogen streaming outward from the Sun, and that at the Earth's orbit this plasma has a density typically of the order of 10^3 protons cm.$^{-3}$ and a velocity of approximately 500 km. sec.$^{-1}$. During periods of violent solar activity the velocity increases possibly to 1,500 km. sec.$^{-1}$ and the density increases by one or two orders of magnitude. Parker[2] has also shown that for theoretical reasons there is a hydrodynamic expansion of the solar corona, referred to as the 'solar wind', and that at the Earth's orbit the solar wind has approximately the same density and velocity as estimated by Biermann.

The interaction of a solar corpuscular emanation with the geomagnetic field is exceedingly complex, and for many years it has been invoked as the basic mechanism for explaining a wide variety of geomagnetic, auroral, and upper atmospheric phenomena. Yet apart from the deflexion of comet tails there is singularly little direct observational evidence in support of the solar-wind hypothesis. The purpose of this communication is to direct attention to some additional observational evidence which supports the idea that there is an interplanetary plasma streaming away from the Sun with a velocity close to that estimated by Biermann and Parker.

Since the pioneer work of Chapman and Ferraro[3], it has been agreed generally that the effect of a solar wind impacting against the geomagnetic dipole field is to compress the field into a radius, variously estimated by different authors, of 5–15 Earth radii on the Sun's side of the Earth. Until recently, there was rather less agreement on the subject of what happens to the geomagnetic field on the night-side of the Earth. It now seems with reasonable certainty that some of the magnetic flux from the polar regions, above the auroral latitudes, is carried round to the night-side and the flux-lines are stretched away from the Earth by the solar wind[4]; this 'arch' of polar magnetic flux does not rotate with the Earth or with the magnetic field at lower latitudes. Some of the flux-lines originating from the geomagnetic polar regions are entangled and embedded in the solar wind[5], and are carried away[6] as a "wind carries smoke from a chimney stack", and thus form[7] a 'magnetic tail' to the Earth. Piddington[7] has also made the interesting suggestion that the gegenschein is located within the Earth's magnetic tail.

The gegenschein, or counterglow, is a faint patch of light in the night sky close to the ecliptic and directly opposite the Sun. Visual[8,9], photometric[9–11] and spectroscopic[9,12] observations by the Russian workers Astapovitch, Divari, Fesenkov, Karimov and Rozhkovski have established that the gegenschein glow is elliptical in shape and has a size roughly of 10° by 6°, with the major axis lying nearly along the ecliptic; that it has short- and long-term fluctuations in size and brightness which apparently have some correlation with solar, auroral and airglow activity; that its position as determined by parallax measurements is variable and is at a mean distance of 20 Earth radii; that its emission spectrum in the visible range consists principally of lines common to the night airglow; and that it has a small but variable displacement to the west of the midnight meridian amounting to a mean value of 3°. Roach and Ross[13] have made photometric studies, and conclude that the gegenschein and the adjacent zodiacal light are due to separate and distinct concentrations of particles. It thus appears that the known properties of the gegenschein are consistent with the idea of a slightly luminous magnetic tail to the Earth, and that the magnetic tail is in fact also the gaseous tail proposed by Arrhenius, Houzeau[14] in 1888, and later discussed by Evershed[15] in 1902. The luminosity is presumably owing to the presence of atmospheric-type atoms which, initially, have migrated along the polar flux-

lines as ions and become entrenched in the magnetic tail.

Since the Earth has an orbital velocity of $v_e = 30$ km. sec.$^{-1}$, it is immediately obvious that a solar wind of velocity v_r streaming radially away from the Sun will form a magnetic tail which is directed to the west of the midnight meridian, and if the angular displacement is α, then :

$$v_r = v_e \cot \alpha \qquad (1)$$

Using the observed value of $\alpha = 3°$ it follows that the solar wind has a mean velocity of 600 km. sec.$^{-1}$. This velocity is remarkably close to the value estimated by Biermann and Parker.

On looking for alternative possible causes of the gegenschein displacement one notices that if neutral atmospheric molecules are ejected, by some unknown means, from the Earth at a velocity v in a direction away from the Sun, the conservation of angular momentum gives a westward displacement of :

$$\alpha = v_e r/vR \qquad (2)$$

for $r \ll R$, where R is the radius of the Earth's orbit and r is the distance of the molecules. For r equal to 20 Earth radii, and v equal to 1 km. sec.$^{-1}$ corresponding roughly to the mean speed at a temperature of 10^3 °K., one finds that α is 3° as required. However, it would seem that the main weaknesses with this explanation are : first, that α is proportional to r, and therefore a gaseous tail observed from the Earth would tend to spread westward in a noticeably asymmetric way ; secondly, that a large distribution in the values of v would mar the possibility of a definite and confined region of luminosity ; and thirdly, it encounters the hitherto unsolved problem of the gaseous tail theories of accounting for a practically non-divergent jet of gas[16].

In all probability the solar wind at the Earth's orbit is not directed entirely radially from the Sun, and therefore equation (1) must be modified to :

$$v_r = (v_e - v_\perp) \cot \alpha \qquad (3)$$

where $v_\perp$ is the transverse velocity of the solar wind at the Earth's orbit in the direction of the Earth's orbital motion. If the angular momentum of the solar wind is conserved from the inner corona, the transverse velocity at the Earth is 0·01 km. sec.$^{-1}$ and is too small to affect noticeably the position of the gegenschein. But if the solar wind and the Sun are electromagnetically coupled[17] and tend to rotate together, the maximum possible distance from the Sun for co-rotation is 0·17 of the radius of the Earth's orbit, and corresponds to the Kepler orbit in which the angular velocity is that of the Sun. In this case the transverse velocity at the Earth is 12 km. sec.$^{-1}$, and according to equation (3) the solar wind has therefore a radial velocity of 360 km. sec.$^{-1}$ for a displacement of 3°.

It must be admitted that our present knowledge of the gegenschein is inadequate and is far from being in a satisfactory state. The little that is known, however, is not inconsistent with the idea of a solar wind interacting with the geomagnetic field and producing a slightly luminous gas-magnetic tail to the Earth. Therefore, if it is accepted that (1) the solar wind carries away a magnetic tail from the Earth, and that (2) the gegenschein is a luminosity associated with the magnetic tail, then the characteristic westward displacement of 3° confirms that the solar wind has a mean velocity close to 500 km. sec.$^{-1}$.

E. R. Harrison

Atomic Energy Research Establishment,
Harwell, Didcot.

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Existence of Net Electric Charges on Stars

Prof. V. A. Bailey has recently proposed[1] an equation relating the electric charge on a star to the Newtonian gravitational constant and to the mass of the star. This equation has the form :

$$Q = \beta G^{1/2} M \qquad (1)$$

where Q is the electrostatic charge, β is a dimensionless constant of approximately 0·03 for the Sun, G is the gravitational constant, and M is the mass of the star. For the Sun, Q turns out to be $1{\cdot}5 \times 10^{28}$ e.s.u. I wish to point out that equation (1) is closely related to a similar equation which I have obtained for the gravitational fields in the interior of fundamental particles (electrons and protons) by applying the Weyl theory of gauge invariance to the Einstein–Ricci curvature tensor.

Since in the original Weyl theory the dimensions of a charged particle change as it moves from point to point in an electromagnetic field, it is necessary to alter this theory by imposing two constraints if it is to lead to results with physical meaning[2]. The first of these constraints limits the motion of the particle to that path between any two points along which the total change in the dimensions of the particle is a minimum. This at once leads to the Lorentz ponderomotive force. The second constraint limits the possible paths still further by requiring that the dimensions of the particle take on their initial values when the particle returns to its starting point. This gives us the Bohr–Sommerfeld quantum condition.

If one[3] now enlarges the Einstein–Ricci curvature tensor by imposing the condition that it be gauge invariant, the additional terms that are obtained are related to the electromagnetic 4-vector and Maxwellian field. If an invariant is constructed with this enlarged tensor, and this is then taken as the Lagrangian density, one obtains the second-order Dirac equation as written down by Feynman and Gell-Mann[4] provided the radius of Gaussian curvature in the neighbourhood of the electron is placed equal to the Compton wave-length $\hbar/mc$.

Since the formula for the Gaussian curvature contains the gravitational constant G as a factor, one is thus led to the following equation for G inside an electron (or proton):

$$G = \hbar c/m^2 = \alpha^{-1}(e/m)^2 \qquad (2)$$

where α is the fine structure constant, $e^2/\hbar c$, and e is the electronic charge. Thus the value of the gravitational constant inside an electron is of the order of 10^{24} c.g.s. units.

If we take the square root of (2) we obtain Bailey's equation for the Sun:

$$G^{1/2} = \alpha^{-1/2}(e/m) \qquad (3)$$

provided we identify his constant β with the square root of the fine structure constant, $e/(\hbar c)^{1/2}$. Of course, the two quantities are numerically different, but that is simply because the quantity that we must use in place of $e/(\hbar c)^{1/2}$ if we wish to apply (3) to the Sun is:

$$\beta = Q\,(2I\omega c)^{1/2} \qquad (4)$$

where I is the moment of inertia of the Sun, ω is its angular velocity, and c is the speed of light.

In other words, what is significant in formula (3) is not the appearance of Planck's constant but rather the appearance of an angular momentum. If we are to apply (3) to the Sun, we must introduce a kind of 'fine structure constant' corresponding to the angular momentum and charge of the Sun.

If in (4) we introduce Bailey's value for Q and use the value of I obtained from calculations of radius of gyration for solar models[5], the value of β is about 0·03 as postulated by Bailey.

What is perhaps more interesting is that (2) leads to the expression relating the mass and the radius of a finite universe as first derived by Einstein in 1916. If we consider the universe as a closed system with intrinsic angular momentum $I\omega$, then the radius R of the universe must be such that $R\omega = c$ or $\omega = c/R$. If we now take I to be kMR^2, where k is a numerical factor approximately unity, then the expression for G for the universe as a whole becomes:

$$G \simeq I\omega cM^{-2} = kRc^2M^{-1} \qquad (5)$$

This is just Einstein's formula for a universe of radius R and mass M. It is interesting to note that an equation of the form (2) has been suggested by Chandrasekhar[6] as the most general combination of the constants $\hbar$, c and G, and the mass of the proton.

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PROF. MOTZ'S model of an electrically charged fundamental particle is of particular interest because it directly contradicts the commonly held view that gravitational fields on the atomic scale are quite negligible. By means of some bold but simple hypotheses he appears to obtain a model of an electron (or proton) which is capable of holding its parts together against the electric forces of repulsion between these parts.

Prof. Motz's comparison of his equation (2) with my equation (1) is also of interest, because it extends the similarity between astronomical systems and atomic systems which was first demonstrated by Bohr and Sommerfeld's theories and their extension by Goudsmit and Uhlenbeck; but here the similarity is one between single constituents of these two kinds of systems.

It is remarkable that the order of magnitude 0·03 for the pure number β in the equation (1) is consistent with the values derived by Motz from his table of solar models published in his ref. 5. It should, however, be noted here that on reconsideration of the data on which I based my first estimate of β, I have recently reduced its value to about 0·006 and correspondingly reduced the Sun's charge to about -3×10^{27} e.s.u. But the uncertainties in the data make even this recent estimate merely one of order of magnitude.

In a recent communication[1] on the apparent steady component of the interplanetary magnetic field, it is shown that the findings of the magnetometer on the space probe *Pioneer* I during the first 50 days of operation strongly support the hypothesis that the Sun carries a large negative charge. But from that communication it may be inferred that in order to determine the value of β experimentally in this way it would be necessary to make measurements by means of instruments carried in space probes moving in different orbits. Such a determination of β is highly desirable, since it would be not only of interest to astronomers but also might be of value in connexion with Prof. Motz's considerations.

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PHYSICS

Effect of Dissolved Air on the Viscosity of Water

WATER at 20° C. is now widely used as the primary standard for viscosity measurement[1], the viscosity being taken to be 0·01002 poise as obtained by Swindells, Coe and Godfrey[2], and confirmed by Roscoe and Bainbridge[3]. The International Organization for Standardization has recently proposed the international adoption of this value, but the question has arisen whether the viscosity depends significantly on the presence of dissolved air in the water[4]. We have now made some very accurate measurements to determine the effect of dissolved air, and found it to be insignificant for present standards requirements.

The viscosity of air-saturated water has been measured relative to that of air-free water. The measurements were made using sealed suspended-level viscometers incorporating fine platinum contacts by means of which electronic timing equipment is triggered. The viscometers were immersed in a stirred water-bath, the temperature of which was kept constant to within ± 0·0007 deg. C. by a proportioning controller and measured with a platinum resistance thermometer. Within a set, the concordance of flow-times was 1 part in 50,000.

The ratio of the flow-times obtained at 20° C. with and without air at atmospheric pressure in the viscometers was found to be 1·00125 ± 0·00009 at a 95 per cent confidence-level. To obtain the corresponding ratio of kinematic viscosities, this figure must be reduced by 4 parts in 100,000 for the effect of the pressure difference on the dimensions of the viscometers, and by a factor of 1·00119 for the effect of the buoyancy of the water with respect to the water-saturated air. The resulting viscosity ratio does not differ significantly from unity. More specifically, the effect of air at atmospheric pressure on the kinematic viscosity of water does not exceed 13 parts in 100,000 at the 95 per cent confidence-level. This statement relates to the combined effects of the dissolved air and the pressure; but it can be shown independently, by extrapolating data available for higher pressures, that the direct effect of a pressure of one atmosphere is to change the viscosity by no more than a few parts in 100,000.

Likewise, at 25° C. and 30° C. no significant effect was found.

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A Phenomenon in *n*-Hexane prior to its Electric Breakdown

A PRELIMINARY photographic study has been made using a schlieren optical system in which a 1-microsecond flash-light source was arranged to flash five times in synchronism with a single-step function voltage applied to electrodes immersed in highly purified *n*-hexane. The events were recorded with a rotating-mirror camera.

In the examples shown in Fig. 1, the first photograph in each series shows the undisturbed state of the liquid prior to the application of the voltage. Each second photograph, taken 7 μsec. after the application of the voltage, shows that the refractive index in a localized region at the pointed cathode has become different from that in the surrounding liquid. The extent of the localized region was observed to be greater with higher voltages under otherwise similar conditions.

The phenomenon at the cathode can disappear (Fig. 1*A*) without breakdown ensuing, even with the voltage maintained. On the other hand, Fig. 1*B* shows a spark breakdown, which is self-luminous and therefore recorded, about 20 μsec. after the application of the voltage. The later photographs record the bubble originating from the spark. Fig. 1*C* shows similar phenomena in a point-plane gap with the breakdown about 10 μsec. after the application of the voltage.

All these phenomena are detectable with a shadowgraph technique, which is less sensitive than the schlieren technique; thus the refractive index of the region at the cathode must be greatly different from that of the surrounding liquid, but it is not known whether it is higher or lower.

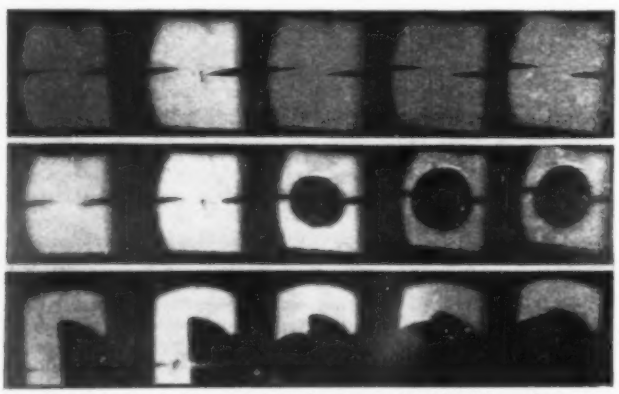

Fig. 1. Synchronized schlieren photographs of pre- and post-breakdown phenomena in *n*-hexane. In each series the first photograph was taken 70 μsec. before the application of a step function voltage, and the remaining photographs were taken, respectively, 7, 80, 150 and 220 μsec. after the application of the voltage. Ratio voltage/gap-length: *A*, 325 kV./cm.; *B*, 335 kV./cm.; *C*, 330 kV./cm.

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Emission of Soft Electromagnetic Radiation from Metals by the Impact of High-Energy Protons and Positive Ions

IT is known that the impact of fast protons[1] and α-particles[2] on metals results in the emission of their characteristic X-radiation. It has not been reported, however, whether ultra-violet and visible radiation are also emitted from metals when high-energy protons and positive ions strike them. Sir J. J. Thomson[3] predicted as early as 1914 that the impact of positive ions on metals may result in the emission of soft electromagnetic radiations. Evidence supporting this view has been given in recent experiments, where it is shown that ultra-violet and visible radiation is emitted when positive ions and protons of moderate energies strike a nickel surface[4]. These experiments have now been extended to protons and positive ions of energies of 400–700 keV.

A proton beam was obtained from an Oliphant ion source[5] of our 1·2-MeV. Cockcroft–Walton generator, supplied by Messrs. Philips Electrical Co. of Eindhoven, Holland, and described earlier by one of us[6]. It was analysed with a 15° permanent magnetic analyser using an adjustable magnetic shunt. The voltage for the ion source was obtained from a 0–50-keV. transformer energized by a remote controlled 0–220-V. a.c. generator driven by a large insulating belt, both installed in the top of the accelerator along with the Oliphant discharge tube and the gas reservoir.

The output voltage of the transformer was rectified with a Philips high-tension five-ring mercury rectifier valve and was stabilized with an R.C. filter, and the gas-flow to the ion source was regulated by a remote-controlled needle valve. The discharge was run at 10–20 m.amp. with discharge potential of 20–30 kV. Protons travelled through a long metal tube cooled with liquid air and entered the target chamber through a narrow aperture before striking the target 10 cm. below. The main accelerating column was exhausted with a large diffusion pump backed by a Kinney pump. A separate set of these pumps evacuated the proton-collimating tube and the target chamber through a large liquid-air metal trap continuously during experiments.

Observations were taken with proton current varying from $1{\cdot}0 \times 10^{-7}$ amp. to $4{\cdot}0 \times 10^{-6}$ amp. Radiation emitted from the target was detected with a photoelectron E.M.I. multiplier type 6260 and with associated electronic equipment, and was studied with Kodak gelatine filters supplied by Kodak, Ltd., of London.

It was observed that soft electromagnetic radiation in the visible and ultra-violet regions is emitted from a nickel target, in a well-degassed as well as in an un-degassed condition. The intensity of the radiation in the ultra-violet region above 3300 Å. was greater than that of the visible part of the spectrum in either case. The total intensity of the radiation of wave-length above 3300 Å. rises more rapidly than the increase in the proton current and is always greater from a dirty surface than from a clean one. It shows, however, a decrease of about 20 per cent as the energy of the protons is raised from 400 to 700 keV. at a constant proton current. The spectrum in the visible region was continuous, with a pronounced flat peak between 4600 and 4900 Å. Radiation of wave-length above 5200 Å. was not measured, however, on account of experimental limitations. A spot visible to the naked eye appears on the target with as small a current as $1{\cdot}0 \times 10^{-7}$ amp.

In one set of experiments the target was well degassed under high vacuum by electron bombardment at bright red heat for several hours before observations were taken. The degassed target was left under vacuum overnight and observations were repeated the following day after degassing it again, when the results were found to be reproducible.

Experiments have also been performed with unresolved hydrogen ions obtained from a 30-Mc./sec. radio-frequency source recently installed in our accelerator. Hydrogen flowed from the gas reservoir to the radio-frequency discharge tube through a remote-controlled nickel valve the temperature of which determined the gas-flow and thus the discharge pressure. The voltages for the focusing lens and the ion-extracting probe were obtained from 50-kV. and 5-kV. selenium rectifier Cockcroft–Walton cascade sets, respectively, which were both remote controlled and were placed in the top of the accelerator with the power supplies for the 30-Mc./sec. oscillator. The positive ion current to the target was adjusted by varying the pressure of the discharge gas or the voltage of ion-extracting probe or both and was varied from 4×10^{-6} amp. to $15{\cdot}0 \times 10^{-6}$ amp. while the energy of the ions was kept at about 400 keV. We have observed that the radiation emitted from the nickel target, both from its dirty and clean surfaces, gives a continuous spectrum in the visible region in this case also. The spectral intensity distribution curve is flat from 4000 to 4700 Å., beyond which it falls rapidly. The intensity of the visible radiation with current of 10×10^{-6} amp. and above was too high for direct measurement, and Kodak neutral density filters were used to cut it down for recording with the electronic circuits. In one set of observations the ion current was raised to a value high enough to make the target glow bright red due to bombardment when it was kept under this condition for several minutes for degassing, and was then suddenly decreased to about 4 μamp. for taking observations from a clean surface freshly prepared.

We have checked that the radiation detected by us is not due to the secondary electrons emitted from the edges of the aperture by the protons entering the target chamber, nor is it due to their heating effect on the nickel target. Details of the experiments will be published elsewhere.

We are indebted to Sir John Cockcroft and to Sir Mark Oliphant for advice and encouragement, and to Dr. Paul W. McDaniel, director of the Research Division, U.S. Atomic Energy Commission, for helpful discussion and suggestions. We also thank the U.K. Government for the gift of high-tension selenium rectifiers and the 30 Mc./sec. radio-frequency ion source recently installed in our accelerator under the Colombo Plan.

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Flow Patterns in Particle Beds

The technique of observing gas-flow patterns in fluidized beds described in a recent communication[1] is a useful contribution to the methods available for investigating fluidization behaviour. A comparable technique has been developed here using dye injection for tracing the flow pattern of water passing through particle beds. Though this technique was found useful in the pre-expansion stage, it was the reverse during bed expansion when it actually tended to mask the interesting phenomena shown in Fig. 1. These photographs were taken by transmitted light without the use of dyes, and show the activation of a bed of 100μ glass spheres by water. Local bed expansion or increased voidage is indicated by increase in transmitted light. Photograph *C*13 shows the approximate steady-state conditions in a bed which, viewed superficially, has all the appearance of uniform and smooth particulate fluidization. The series *A*1–*A*12 (of which *A*1, 3, 6 and 12 are reproduced) shows the development of a flow pattern in the same bed at a much lower superficial water velocity. The last of that series again approximates to steady-state conditions, the only changes thereafter being a slow meandering of the flow channels. Not seen in the photographs but observed visually are occasional series of mushroom-shaped low-density discontinuities rising in one or more of the channels.

The visual study of particle bed activation by air was studied here in a parallel-plate apparatus using

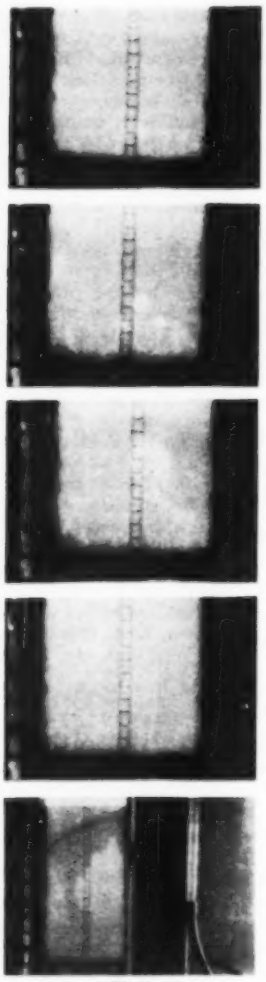

Fig. 1

mixtures of particles with differently coloured size ranges. It was possible to observe the circulation of 300-mesh particles of alumina dyed red, within air bubbles held stationary by stiction effects in a bed of 100 mesh undyed alumina. A modification of this apparatus, suitable for water fluidization, was made with the prime object of investigating what appeared to be anomalous and hitherto unreported behaviour, namely, an apparent bubbling stage in water fluidized beds of small, moderately dense particles. In all cases studied, the expansion from fixed bed to particulate fluidization passed through a stage closely resembling the gentle bubbling stage in air fluidization. Streams of mushroom-shaped pseudo-bubbles can be observed rising in narrow channels within water-activated beds of alumina and glass spheres within the size range of 60–200μ, but it is not clear whether these are of the same nature as bubbles in air-activated beds, or some type of vortex phenomenon. In the case of glass spheres larger than 1 mm. diameter, horizontal striation can be observed with low-density strata being propagated upwards continuously and evanescing at the top of the bed. These occasionally break and re-form, giving an appearance of mushroom-shaped bubbles.

The term 'parvoid' is suggested as a generic term to describe these and other low-density discontinuities in fluid-activated beds. With 2-mm. glass spheres, parvoids of mushroom shape ranging from 1 cm. to 5 cm. in width can be seen rising at some 5 cm. per sec. through the dense bed at superficial water velocities of some 2 cm. per sec. These parvoids give the impression of being completely void of particles, in contrast to parvoids in beds of smaller particles.

The possible existence of discontinuities and non-uniformity in what have hitherto been considered to be homogeneous beds may have some relevance to much published work in the literature. A complete account of these discontinuities with a tentative theory as to their formation and relationship to fluidization behaviour will be published elsewhere. There is evidence that what is known as particulate and aggregative fluidization may be occurring at one and the same time in a fluidized system, and that it is the proportion in which they occur that defines the one type of fluidization as against the other. If this is so, one could expect a transition from one to the other in any fluid-activated particle system, as the fluid velocity is increased in stages.

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BIOPHYSICS

Molecular Sieve Behaviour of Dental Enamel

Normal mammalian tooth enamel is highly calcified, containing 97 per cent mineral and 3 per cent organic material and water. The mineral is hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$, and it is associated with a protein constituent of the keratin type[1]. From histological studies it is well known that normal enamel is made up of structural units which are prismatic in shape and contain mainly crystallites of hydroxyapatite. The organic constituent is concentrated at the margins of these prisms but it is also present in smaller amounts within them. In the prisms the crystallites are highly oriented, with their optic (fibre) axes approximately parallel with the longitudinal axes of the prisms. This submicroscopic structure of normal enamel is shown diagrammatically in Fig. 1. The fully formed enamel can be broken down either *in vitro* by organic acids such as lactic acid, or *in vivo* by the processes concerned in carious decay. In each case the mineral is gradually dissolved out until, eventually, the structure of the enamel is destroyed[2].

Since hydroxyapatite is a uniaxial mineral possessing negative birefringence, normal enamel shows a negative intrinsic birefringence relative to the longitudinal axis of the prism due to this inorganic component. This is the only birefringence shown by normal, fully formed enamel. However, during both formation and acid breakdown of normal enamel, it has been shown that a considerable number of freely accessible spaces exist between the crystallites in the prisms, and these spaces can give rise

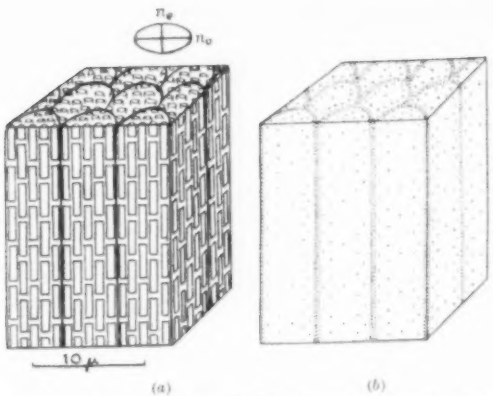

Fig. 1. Diagrams illustrating the fine structure of normal tooth enamel. (*a*) The arrangement of mineral elements. The enamel consists of columnar prisms within which are tightly packed, rod-shaped crystallites of hydroxyapatite. The index ellipse of the crystallite system is indicated by the axes n_e and n_o. (*b*) The distribution of organic elements. A keratin-like protein material is concentrated around the margins of the prisms, but smaller amounts occur throughout

to an additional optical effect. A system of rod-shaped elements, such as crystallites, separated from each other by spaces containing a medium of different refractive index, constitutes a 'mixed body'[3]. A rodlet mixed body produces positive form birefringence relative to the direction of orientation of the rods. It follows, therefore, that enamel which is being formed or which is undergoing breakdown will show negative intrinsic birefringence due to its oriented inorganic component and positive form birefringence due to the intercrystallite spaces[4].

The strength of the positive form birefringence depends on the difference between the refractive indices of the crystallite material ($n = 1{\cdot}62$) and that of the medium occupying the spaces between the crystallites. The latter may be altered by the inclusion in these spaces of, for example, air ($n = 1{\cdot}0$), water ($n = 1{\cdot}33$), organic liquids such as alcohols ($n \sim 1{\cdot}4$) or quinoline ($n = 1{\cdot}62$)[3]. Quinoline has the same refractive index as the crystallite material. If it is used as the imbibing medium, form birefringence will not be produced and only the negative intrinsic birefringence of the mineral will be apparent. If the spaces are occupied by a medium of lower refractive index than this, then the result will be a summation of the positive form and the negative intrinsic birefringences. With media of refractive index 1·45, these opposing effects tend to compensate each other so that the system shows no activity between crossed polars. With media of lower refractive indices than this, the positive form birefringence predominates.

Using this method it has been possible to examine the nature of the spaces present in certain parts of the carious lesion (Fig. 2), and it has been found that the body of the lesion, which develops at a relatively late stage in the attack, behaves in exactly the way described[1]. However, one of the earliest stages of the carious lesion is the appearance of an opaque zone when examined in Canada balsam. This is the so-called dark zone. The development we wish to report concerns the detailed structure of the dark zone and the determination of the relative sizes of the spaces which are present, by showing that the extent of inclusion of organic liquids into these spaces depends on their molecular dimensions. It should, perhaps, be pointed out that whatever the size of spaces in the dark zone, the total volume of spaces is very small[5].

The dark zone is observed only in certain circumstances, for example when a tooth section is examined in media such as Canada balsam or quinoline (Fig. 2). It is also seen when a section is examined in air, but is not easily distinguished because it is concealed by the form birefringence of the neighbouring parts of the lesion. The dark colour of the zone as seen in transmitted light, as well as the strong positive birefringence seen between crossed polars, must be due to the fact that the intercrystallite spaces contain air. This suggests that the occurrence of the zone in sections mounted in Canada balsam or in quinoline is because the molecules of these liquids are too large to be included in the spaces.

This hypothesis has been subjected to experimental scrutiny by examining the optical behaviour of sections of carious lesions in enamel which were first dried and then allowed to imbibe, in turn, the liquids listed in Table 1. The results of a typical experiment are recorded there.

It will be noticed that the degree of observed birefringence becomes progressively more positive as the series of normal (straight-chain) alcohols is ascended from methyl alcohol to *n*-octyl alcohol. This effect cannot be due to differences in the refractive indices of the alcohols since the refractive index is approximately the same in each case. In fact the refractive indices do show a slight increase as the series is ascended.[6] If the changes in refractive index had been influencing the total birefringence, then this would have produced a trend opposite to that observed. It therefore follows that this change in positive birefringence in the series, methyl

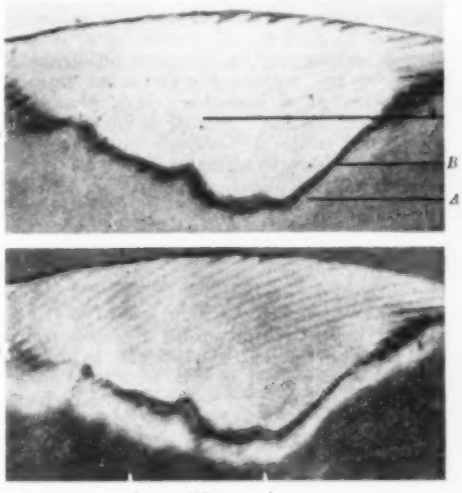

Fig. 2. Section of human permanent enamel mounted in quinoline and showing the dark zone around a carious lesion. (*a*) Appearance of the section in transmitted light. The lesion is advancing into the enamel, its front being indicated by the so-called translucent zone (*A*). Within the translucent zone is the deep brown, opaque 'dark zone' (*B*), and within this again is the body of the lesion (*C*). (*b*) Appearance of the same area of enamel between crossed polars. The dark zone shows up as a narrow band with positive birefringence and is delineated on either side from neighbouring areas by black lines of compensation. The rest of the enamel has negative birefringence

Table 1

Medium	Refractive index	Observed birefringence $\times 10^4$
Methyl alcohol	1·33	11·97
Ethyl ...	1·36	10·00
n-Propyl ...	1·38	7·33
n-Butyl ...	1·40	5·85
n-Pentyl ...	1·41	4·84
n-Hexyl ...	1·42	2·23
n-Heptyl ...	1·42	4·11
n-Octyl ...	1·43	5·85
Allyl ...	1·41	9·71
*Iso*propyl ...	1·37	3·89
Tert.-butyl ...	1·38	11·29
Sec.-butyl ...	1·39	11·97
Tert.-amyl ...	1·41	12·59
Water ...	1·33	13·01
Quinoline ...	1·62	13·21

n-octyl alcohol, is due to changes in the extent of replacement of air ($n = 1·0$) by alcohols ($n \sim 1·4$) in the intercrystallite spaces. As the homologous series is ascended, the molecular size of the alcohols increases. It is suggested that, with any particular alcohol, spaces larger than a certain critical size can be occupied by the alcohol, whereas spaces smaller than this size cannot be occupied and will still contain air. In all the many specimens examined to date, a dark zone has never been observed in methyl alcohol. It may therefore be concluded that the smallest size of intercrystallite space so far detected is such as to allow the inclusion of molecules of methyl alcohol.

It has also been shown (Table 1) that branched-chain alcohols (for example, *iso*propyl or *tert.*-butyl alcohols) are included to different extents from the corresponding normal alcohols. This suggests that the ease of penetration depends not only on the linear dimensions but also on the cross-sectional areas of the intercrystallite spaces.

It should be emphasized that there is a variation in the sizes of the intercrystallite spaces so that with the higher alcohols only large spaces can be occupied, whereas with alcohols of smaller size, a greater number of spaces can be occupied. The extent of inclusion of the various liquids is an interesting demonstration of a molecular sieve phenomenon[6] in a biological system. Similar behaviour has also been observed in the non-carious tooth enamel of a variety of vertebrate animals. In each case the tissue showing the phenomenon appears to contain slightly less mineral than the fully formed normal enamel.

The significance of these results in relation to the understanding of the processes of carious breakdown will be discussed elsewhere[7].

This work was carried out while two of us (K. V. M. and D. F. G. P.) were in receipt of grants from the Medical Research Council, to which thanks are offered.

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Thread-like Reticulum in Latex from *Hevea brasiliensis* and its Relation to Latex Particles

In a previous communication[1] I directed attention to the complexity of the 'lutoids' separated from fresh latex by high-speed centrifuging. I have now made further studies of fresh latex using phase microscopy. As reported in the literature[2–4], aggregates of lutoids occur in untreated fresh latex; I now find these aggregates not only contain lutoids, but also Frey Wyssling[5] particles and pear-shaped rubber particles, all of which occur in a gelatinous matrix. Associated with this gelatinous material, I have observed many very fine threads which often trail from the edges of the aggregates. These are quite distinct from the chains of coagulated rubber which have been reported in latex under certain conditions. Since the particles differ in density, the effect of high-speed centrifuging on the aggregates will be disruptive.

Latex was collected into chilled glass vessels and centrifuged under refrigerated conditions into zones by a technique essentially similar to that of Moir[6]. Moir remarks that the (middle) serum fraction often has a 'ropey' appearance to the naked eye. I now find this is due to many long thread-like processes beaded with particles including lutoids, Frey Wyssling particles, a few rubber particles and many particles too small to be identified. The Frey Wyssling particles commonly occur in grape-like clusters. In positions corresponding to Moir's zone 2 and zone 11 are found patches of translucent jelly. The zone 11 jelly at the bottom of the tube contains many particles, especially lutoids, and sometimes portions of plant tissue. The zone 2 jelly in the upper half of the tube contains threads to which many rubber particles are attached. The general appearance is that of fruit growing from a branch. Pear-shaped rubber particles are attached by their stalk-like narrow ends. Apparently the aggregates seen in untreated latex have been torn apart, rubber particles moving upwards and lutoids downwards, with attached threads and jelly parted between them. A portion remains incompletely separated, intermediate in density, and is found in the serum. Frey Wyssling particles are found in all three regions.

Fig. 1. Rubber particles attached to threads in upper (zone 2) fraction. Lutoids and Frey Wyssling particles have been stripped from the threads by the centrifuging. Reichert negative phase, flash illumination. (× c. 2,530)

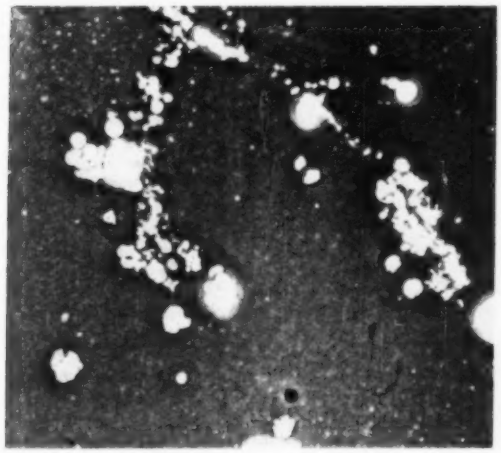

Fig. 2. Partially disrupted aggregates in the middle (zone 5/6) fraction. Rubber, lutoids, clusters of Frey Wyssling particles are still attached. Reichert negative phase, flash illumination. (× *c.* 1,330)

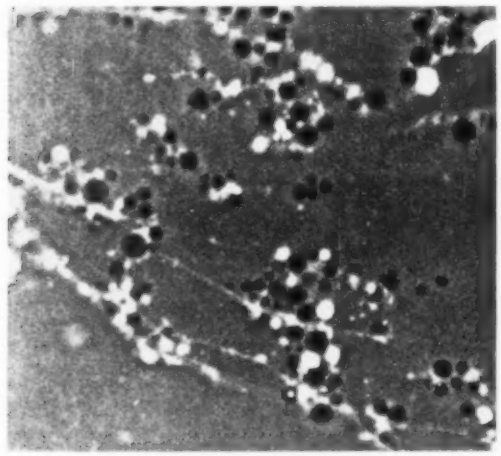

Fig. 3. Lutoids attached to threads in lower fraction from re-centrifuged aggregates. Rubber and most Frey Wyssling particles have been stripped from the threads by the centrifuging. Reichert negative phase, flash illumination. (× *c.* 1,330)

As supposed by Moir[6], zone 8 is predominantly lutoids. Careful examination shows that some of these have short lengths of thread attached, suggesting that they have been torn from the main thread system. By re-centrifuging serum containing partially separated aggregates, I have been able to concentrate such lutoids. Using time-lapse photography I have recorded interactions between thread and lutoid. Over a period of 2 hr. the thread thickens and proves to be tubular, for the spherical lutoid suddenly discharges its contents into the swollen thread, the whole forming an elongated body enclosing captive particles in motion. A similar experiment with a short length of thread studded with very small particles recorded a swelling which formed locally. The small particles were then seen to be freely in motion within the swelling, so that they must have been contained originally inside the tubular thread and not attached to its exterior. The swollen thread had the appearance of a lutoid complete with captive particles.

From these experiments it seems that the aggregates include all three types of particle commonly seen in latex, linked by a reticulum of fine threads now shown to be tubular and sometimes to enclose very small particles in their interior. The whole constitutes a rather jelly-like matrix and is probably a fragment of a more extensive cytoplasmic structure in the latex vessels, carried away by the outflow of latex. Such a reticulum is, of course, a most likely site for particle synthesis. Normal tapping methods must tear many particles free from their attachments even if they are not liberated by other means. Frey Wyssling's observation[5], that the particles called after him often occur in clusters, is confirmed. It now seems that they are formed in this fashion on the reticulum. Similarly the characteristic pear shape of many rubber particles[7,8] follows from their mode of formation, whether or not the aggregation mechanism proposed by Lucas[9] operates afterwards.

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CHEMISTRY

'Ligand Exchange': a Novel Separation Technique

A NOVEL technique for analytical and preparative separations of compounds which can form complexes or adducts with metal ions has been worked out in this laboratory. The new technique can appropriately be called 'ligand exchange'. The method combines two fields of chemistry, namely, ion exchange and co-ordination chemistry, in order to accomplish a task that neither could do alone.

An ion exchanger containing a complexing metal ion (Cu^{2+}, Cu^{+}, Ni^{2+}, Ag^{+}, Co^{3+}, etc.) is used as a solid sorbent. The potential ligands are sorbed from solutions or gases and form complexes with the metal in the resin or displace other ligands which have previously complexed the metal. The latter remains in the ion exchanger. In contrast to conventional ion exchange where counter ions are exchanged, ligand exchange is exchange of ligands for others or for solvent molecules in the ionic solvation shells. Ligands which can be isolated or separated include ammonia, organic amines, polyhydric alcohols, olefins, acetylene derivatives, etc., and anions of organic acids and amino-acids. Separations are preferably carried out in a chromatographic column as in ion exchange chromatography or gas-liquid chromatography. Standard chromatographic techniques—elution development, gradient elution, dis-

placement development, frontal analysis, etc.—can be adapted to ligand exchange.

Ligand exchange has several advantages over other, more conventional chromatographic techniques. First, complex formation is a very strong interaction if the proper metal ion is chosen. This provides a very strong 'driving force' for ligand sorption. Thus, ligand exchangers sorb ligands selectively, utilizing almost their full capacity even when the ligand concentration in the external solution or gas phase is extremely low. In this way, ligands can be very efficiently separated from non-ligands. For example, from 10 litres of a 10-p.p.m. solution of most aliphatic amines, essentially all is sorbed by 1 gm. or less of a cation exchanger in Cu^{2+} or Ni^{2+} form. Secondly, complex formation is a highly specific interaction, much more so than ordinary physical adsorption or ion exchange. Complexes of a metal ion with various, even rather similar, ligands differ greatly in their strength. Hence the ligand exchanger can distinguish rather sharply between such ligands, and outstandingly sharp resolutions in separations of ligands from one another can be obtained even in cases in which conventional sorbents fail. A striking illustration of the specificity of complex formation is the separation of the rare earths by ion exchange chromatography; here, differences in complex-strengths with an eluting or developing agent are used for separating metals. Ligand exchange is a reversal of this technique; differences in complex-strengths with a metal are used for separating complexing agents. For example, with ammonia and an organic diamine, separation factors well above 100 were easily attained. Thirdly, ligand exchange is very flexible since the metal ion giving the best separation can be chosen from a great number of elements.

A unique and particularly useful feature of ligand exchange is the following. In separations of ligands of different co-ordinative valences the selectivity can be adjusted and even reversed at will, simply by varying the total ligand concentration in the external solution or gas phase. Consider, for example, the 'ligand exchange' of a monodentate ligand A (occupying one co-ordinative valence of the metal) for a bidentate ligand B (occupying two co-ordinative valences) with, say, Ni^{2+} as the complexing metal ion:

$$NiA_6 + 3B \rightleftharpoons NiB_3 + 6A \qquad (1)$$

The mass action law for this exchange can be written as:

$$\frac{[NiB_3][A]^6}{[NiA_6][B]^3} = K = \text{const.} \qquad (2)$$

or

$$\frac{[NiB_3][A]^3}{[NiA_6]} = K\left(\frac{[B]}{[A]}\right)^3 \qquad (3)$$

For a given constant concentration ratio of B to A, the right-hand side of equation (3) remains constant. Thus, high total ligand concentration (high value of $[A]$ on the left-hand side) favours the complex NiA_6, and low total ligand concentration (low value of $[A]$) favours the complex NiB_3. By selecting a suitable metal ion one can adjust conditions in such a way that the monodentate ligand is preferentially sorbed from concentrated solutions and the bidentate one from dilute solutions. For example, a bidentate diamine is economically separated from (monodentate) ammonia by selective sorption of the diamine from a dilute mixture by a cation exchanger in metal–ammonia–complex form. The diamine is then recovered from the column by displacement with concentrated ammonia, which yields the diamine in high concentration. No regeneration is required since, after displacement, the resin is again in metal–ammonia–complex form.

Displacement of the complexing metal ion from the resin by ion exchange with other cations in the external solution interferes with ligand exchange. Such ion exchange can be suppressed by choosing a resin with ionogenic groups which hold the metal firmly by partial complexing. In non-ionic ligand exchange, carboxylic acid groups usually offer sufficient protection. If requirements are more stringent, as is the case in anionic ligand exchange, chelating resins such as 'Dowex A-1' (iminodiacetic acid groups) can be used. A possible alternative is the use of an anion exchanger with amino groups. Of course, such protection against ion exchange is achieved at a sacrifice in ligand exchange capacity since the ionogenic groups block co-ordinative valences of the metal ion. For example, with Ni^{2+}, two co-ordinative valences out of six are blocked in resins with carboxylic acid groups, and three in resins with iminodiacetic acid groups.

Ligand sorption by cation exchangers containing complexing metal ions was observed as early as 1954 by Walton[1]. Separations by virtue of differences in complexing strength have occasionally been achieved by other authors[2]. However, it appears that so far the general applicability of the principle, the inherent advantages, and, in particular, the effect of the co-ordinative valences of the ligands have not been recognized.

Separation factors and column performance in ligand exchange operations can be predicted with reasonable accuracy solely on the basis of the tabulated values of the complex-formation constants. Publication of a theoretical treatment and experimental results is anticipated elsewhere.

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Method for studying Thermal Stability of Bulk Thermosetting Polymers

The use of thermosetting polymers in high-temperature applications is increasing rapidly; but data on the thermal stability and degradation characteristics of these materials are very limited. A few investigations employing differential thermal analysis and thermogravimetric analysis have been reported, but the number of polymers investigated is small. Both methods, while very useful in elucidating the kinetics of the degradation process, require a specially prepared sample and are not suited to yield information on bulk polymers. A new experimental technique, termed electro-thermal analysis, for determining thermal stability of bulk thermosetting polymers, will be described briefly.

Previous work with electrical volume-resistivity measurements[1,2] has shown their usefulness in studying reactions and transitions of cross-linked polymers. It has also been shown[3] that a completely polymerized

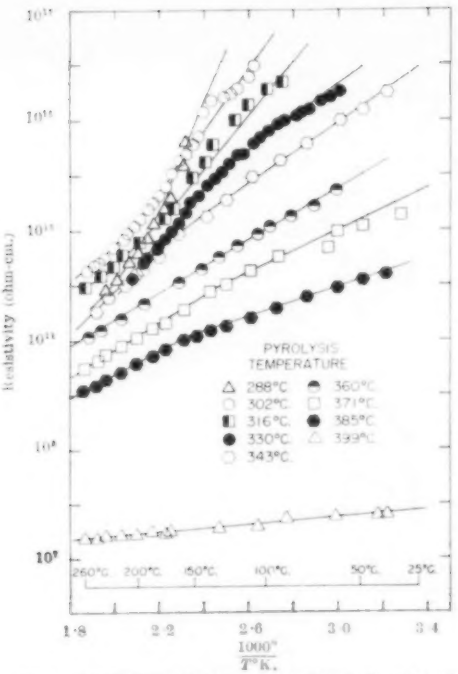

Fig. 1. Temperature-dependence of the electrical resistivity of a thermosetting polymer after pyrolysis for 16 hr. at various temperatures

polymer will exhibit not only the maximum magnitude of resistivity but also the maximum temperature-dependence of resistivity. A cross-linked organic polymer will on pyrolysis exhibit a progressive decrease in these parameters due to degradation, the magnitude of the decrease being approximately proportional to the extent of degradation. At 25° C. the magnitude of the resistivity, $\rho(25°)$, will approach as a limiting value the resistivity of carbon, that is, about 10^{3}–10^{7} ohm-cm., while the temperature-dependence will approach the flat or slightly negative dependence characteristic of carbon. Pyrolysis progressively converts a cross-linked organic polymer into a dense, rigid, extensively conjugated, cross-linked carbonaceous residue[3,4]. This progressive pyrolytic conversion can be measured by resistivity techniques and forms the basis for this investigation. With the exception of a limited study of the structure of several pyrolysates by Winslow and co-workers[3], the use of resistivity measurements in this manner has not been previously reported.

Degradation is determined by repeatedly measuring the temperature-dependence of the resistivity over the range 25–300° C. after each pyrolysis cycle. The arbitrarily chosen pyrolysis cycle is 16 hr. and the temperature is increased about 15 deg. C. for each cycle. Dependence on temperature can be conveniently determined by measuring the resistivity as the pyrolysate is slowly cooled. Onset of thermal degradation is shown by a decrease in the previously established maximum magnitude of resistivity and its dependence on temperature. Pyrolysis is then conducted at progressively higher temperatures until the residue exhibits the electrical properties of carbon. Pyrolysis at still higher temperatures results in graphitization of the carbon and in decreased resistivity[4].

Resistivity measurements are made by a continuous-current monitoring device already described[1]. Parallel-plate electrodes are employed which are completely embedded in the polymer, and pyrolysis is thus conducted in the absence of air. The initial temperature of pyrolysis is a function of the polymer under consideration but will usually be greater than 200° C.

Results obtained by this technique on a fluorinated hydrocarbon thermosetting polymer are shown in Fig. 1. This is a semilogarithmic (Arrhenius) plot of resistivity versus temperature of a polymer after pyrolysis at progressively higher temperatures. This polymer exhibits the maximum values of $\rho(25°)$ and temperature-dependence after heating at 288° C. After pyrolysis at 302° C., a progressive decrease occurs in both parameters. The curve for temperature-dependence becomes almost flat after pyrolysis at 399° C. The large change in $\rho(25°)$ and temperature-dependence between the pyrolyses conducted at 385° and 399° C. suggests that the last significant amount of organic polymer has been burned off, leaving a residue which is almost entirely carbon.

Starting with nickel- and aluminium-doped ion exchange resins, Pohl and co-workers[5] have prepared semiconducting 'pyro-polymers' by this pyrolytic technique.

This technique is used in conjunction with differential thermal analysis and thermogravimetric analysis in investigations of the high-temperature characteristics of various polymers. It is suggested that it be standardized as a test method for determinations of thermal stability on bulk thermosetting polymers. Additional data on epoxide, epoxylated-novolac, polyurethane and silicone polymers together with a discussion of the degradation process in bulk thermosetting polymers will be published later.

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Complexes of Zerovalent Vanadium, Chromium, Molybdenum and Tungsten with a Ditertiary Phosphine

We have previously reported that compounds of type [Mo(diphosphine)$_3$] are obtained from the reaction between dibenzenemolybdenum and the appropriate ditertiary phosphine[1], but we were unable to obtain analogous compounds of chromium by this method. We have therefore developed a direct method of preparation which, in addition to the molybdenum compound, has supplied the $Me_2PCH_2CH_2PMe_2$ complexes of vanadium(0), chromium(0) and tungsten(0) as listed in Table 1. These compounds were obtained by reducing a mixture of the metal chloride and three equivalents of the

ditertiary phosphine in dry tetrahydrofuran. Lithium aluminium hydride (*A*) and sodium naphthalide (*B*) were used to effect reduction.

Table 1

Compound	Colour	m.p. (decomp.)	Reagent	Metal chloride
$[Cr\{C_2H_4(PMe_2)_2\}_3]$	bright yellow	309°	*A* or *B*	$CrCl_3$,3tetrahydrofuran
$[Mo\{C_2H_4(PMe_2)_2\}_3]$	yellow	397	*A* or *B*	$MoCl_5$*
$[W\{C_2H_4(PMe_2)_2\}_3]$	pale yellow	390	*A*	WCl_6*
$[V\{C_2H_4(PMe_2)_2\}_3]$	deep brown	254	*B*	VCl_3

* Reduced in tetrahydrofuran to 3-valent state before addition of ditertiary phosphine.

Reduction appears to be stepwise. For example, the VCl_3-diphosphine solution is deep green, and as reduction proceeds the colour changes through lavender blue to pale brown and is finally deep brown.

The compounds oxidize very quickly in air, and are decomposed by hydroxylic solvents, but have surprising thermal stability. They were purified by recrystallization from hot benzene, in which they are only sparingly soluble. The infra-red spectra of the compounds in 'Nujol' mulls are almost identical. $[V\{C_2H_4(PMe_2)_2\}_3]$ is paramagnetic ($\mu = 2{\cdot}10 \pm 0{\cdot}25$ B.M.), and its electron paramagnetic resonance spectrum is being investigated by Dr. J. F. Gibson of these Laboratories.

A full account of these and of similar compounds of other metals will be published later.

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Stereochemistry of the Succinic Dehydrogenase System

In continuation of work[1-3] on the stereochemistry of Krebs-cycle reactions, the stereochemistry of the succinic dehydrogenase reaction has been investigated with substrates that constrain the enzyme system to demonstrate its stereospecificity. These substrates are L-chlorosuccinic acid, newly found by us, and the L-enantiomorph of methylsuccinic acid; the racemic modification of the latter having been previously demonstrated[4,5] to decolorize methylene blue in the crude heart preparations.

Fig. 1 presents typical kinetic curves obtained by the Warburg technique for the uptake of oxygen by L-chlorosuccinic acid and L-methylsuccinic acid in the presence of Slater's succinic dehydrogenase preparation[6]. It is to be noted that the uptake of oxygen by L-chlorosuccinic acid is of the same order as that for succinic acid while that for methylsuccinic acid is decidedly less. The products of the oxidation were isolated and identified by chromatography[2] from the residue obtained by continuous ether extraction of acidified and deproteinized reaction mixtures. These products were, respectively, chlorofumaric acid and mesaconic acid (methylfumaric acid), thus establishing the dehydrogenation nature of the reaction and the fact that substituted fumaric acids results from the reaction. Of further interest is the fact that D-chlorosuccinic acid has but slight acitivity as a substrate and that D-methylsuccinic acid is not a substrate. The latter compound has

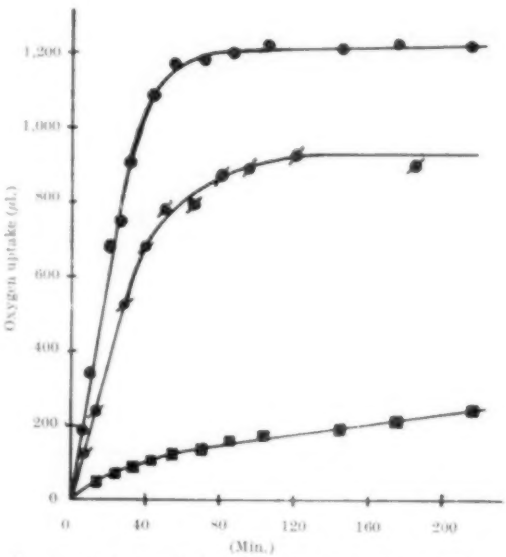
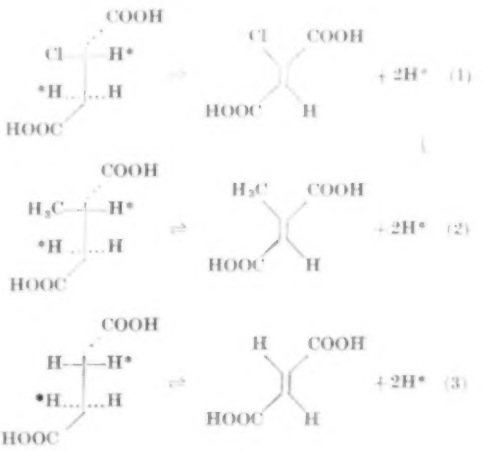


Fig. 1. Warburg oxidation of α-substituted succinic acids by succinic dehydrogenase at *p*H 7·3, 35·5°. Each reaction mixture contained 2·0 ml. succinic dehydrogenase suspension[6] and was 0·056 *M* in phosphate buffer, $6{\cdot}6 \times 10^{-4}$ *M* in methylene blue and 4×10^{-3} *M* in cyanide; total volume, 4·5 ml. ●, 0·018 *M* succinate; ◆, 0·027 *M* L-chlorosuccinate; ■, 0·054 *M* L-methylsuccinate, 85 per cent optical purity

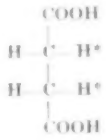
been investigated for inhibitory properties by a spectrophotometric technique[7] and is a competitive inhibitor of succinate oxidation, K_I having the value $1{\cdot}2 \times 10^{-3}$ *M*, at *p*H 7·3 and 35·5°.

It is clear from these results that the succinic dehydrogenase system is, as expected, asymmetric in its action albeit this asymmetry cannot be detected with succinic acid by ordinary techniques[8]. The above results in conjunction with the recently, seemingly conclusive, demonstrated[9] trans-stereoselectivity of the succinic dehydrogenase system permits steric depiction of the reactions, as follows:



where the starred hydrogen atoms are those removed by the enzyme from L-chlorosuccinic acid (1) and L-methylsuccinic acid (2), while for succinic acid (3)

the starred hydrogens are those that are removed from the enzyme-substrate complex, that is, the succinic acid molecule depicted may be rotated 180° around an axis perpendicularly bisecting the bond between the two α-carbon atoms and then placed in the enzyme to yield an enzyme-substrate complex that would lose the two unstarred hydrogens. The two hydrogens that are stereospecifically and stereoselectively removed from the enzyme-substrate complex may be called D-hydrogens, according to the projection formula :



and it is again to be noted that enzymes confer asymmetry on non-asymmetric molecules[10].

It is of interest to note that the succinic dehydrogenase system operates on L-substrates in a *trans* fashion as do *cis*-aconitase[2] and fumarase[3], and that the stereochemistry of the Krebs cycle may now be considered complete since the stereochemical pathway from fumaric acid to *iso*citric acid has been previously traced[3].

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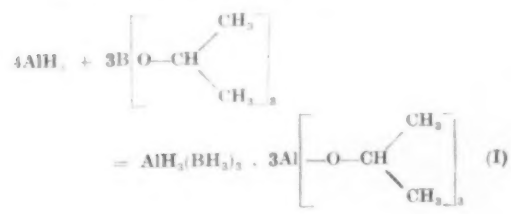
A New Class of the Complex Hydrides

While studying the reaction of aluminium hydride with esters of boric acid, the formation of a new type of the complex hydrides was observed. Thus, aluminium hydride reacts with *iso*propyl borate in ethyl ether, giving rise to a typical representative of the new type of hydride compounds :

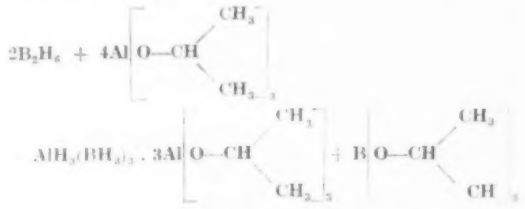


The product is a colourless liquid, distillable *in vacuo* (boiling point at about 120° C. at 0·5 mm. pressure, without decomposition). The yield is about 85 per cent. Analysis : $B_3Al_4H_{76}O_9C_{27}$ (molecular weight, calculated 684·25). B, 4·58 per cent ; Al, 15·7 per cent ; H, 11·05 per cent ; H_{active} (assay by decomposition with diluted hydrochloric acid), 1·79 per cent. C, 45·95 per cent. Calculated values : B, 4·73 per cent ; Al, 15·7 per cent ; H, 11·01 per cent ; H_{active} 1·76 per cent ; C, 47·3 per cent. Complex formation between complex borohydrides and alcoholates is not recorded in the literature, although the possibility of the formation of mixed crystals of lithium borohydride with lithium methoxide has already been considered[1].

The nature of the bonding in these new complexes is not known ; their structure assigned above is confirmed by an alternate synthesis of (I) by the reaction of aluminium borohydride[2] with aluminium *iso*propoxide in tetrahydrofuran. Borane aluminium alcoholate is proposed as a generic name for these compounds. Thus (I) is borane aluminium *iso*propoxide. These compounds display a varying degree of sensitivity to air ; they are handled preferably under pure nitrogen. The reaction is analogous to that of aliphatic or alicyclic borate esters, but with borate esters of phenols a different reaction occurs :

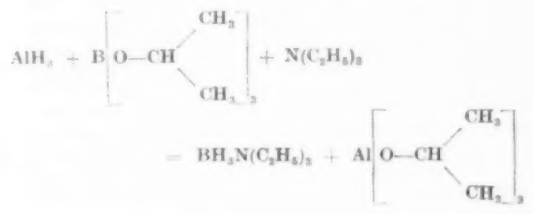
$$2AlH_3 + 2B(—O—C_6H_5)_3 = B_2H_6 + 2Al(—O—C_6H_5)_3$$

The diborane formed evolves from the ethereal reaction mixture after warming it up to 35° C. in a yield of about 70–80 per cent. Compounds of type (I) can be obtained with a 'reversed' method also. For example, diborane and aluminium *iso*propoxide react in tetrahydrofuran, giving rise to (I) and *iso*propyl borate :



This reaction is similar to that of diborane with the alcoholates of the alkaline metals[3].

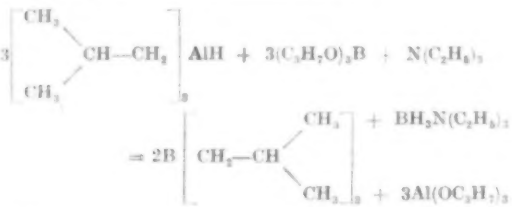
Sodium methoxide and lithium ethoxide give, with diborane, lithium borohydride and sodium borohydride, respectively. H. I. Schlesinger and co-workers treated aluminium alcoholates with diborane gas, but, using solid alcoholates, they obtained in a partial reaction an uncharacterized mixture of different products. The presence of amines completely changes the picture. Thus, aluminium hydride gives, with borate esters, in the presence of triethylamine triethylamine-borane (yield about 75 per cent) and aluminium alkoxide :



Borane aluminium *iso*propoxide is a strong reducing agent. It reduces many types of organic and inorganic compounds, for example, the carbonyl compounds to the corresponding alcohols, the esters to the primary alcohols, the nitriles to the amines. Its reducing strength probably equals the strength of aluminium borohydride. What seems important is that it is soluble and can be used in a broad range of solvents, for example, hexane, ligroin, mineral oil, ethyl ether, chloroform. No other hydride-type reducing agent is soluble in such a broad range of solvents.

The covalent, non-salt-like character and the strong reducing ability of these compounds agree with the correlation recognized earlier between these properties of the complex borohydrides[4].

As I found, the reaction of aluminium alkyl hydrides with borate esters gives products indicating that these compounds behave as mixtures of aluminium hydride and aluminium alkyls. For example, di-*iso*butyl aluminium hydride in the presence of triethylamine reacts with *iso*propylborate, giving rise to tri-*iso*-butylboron and triethyl amine borane[5]:



The complex aluminohydrides, for example $LiAlH_4$ and $NaAlH_4$, are transformable also, by treating them with borate or metaborate esters, to the corresponding borohydrides:

$$LiAlH_4 + B(OR)_3 = LiBH_4 + Al(OR)_3$$

The yields are 70–90 per cent; patients have been applied for.

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BIOCHEMISTRY

Evaluation of the Activity of Corticosteroid 11β-Hydroxylase

2-Methyl-1,2-*bis* (3-pyridyl)-1-propanone (*SU* 4885) has been introduced as an agent for assessing pituitary–adrenal integrity and pituitary reserve[1]. The action of *SU* 4885 is to inhibit 11β-hydroxylation on the corticosteroid nucleus[2,3]. Administration of *SU* 4885 in the presence of a normal pituitary–adrenal relationship results in an increased excretion of 17,21-dihydroxy-20 ketosteroids as measured by the Porter-Silber[4] and ketogenic steroid reactions[4]. This increase is a resultant of the combined effect of decreasing 11β-hydroxylation, presumably increasing adrenocorticotrophic hormone production and increasing the production of 11-deoxycorticosteroids.

Since the inhibition of 11β-hydroxylation is not complete, situations may arise where there may not be a marked change in the total corticosteroid excretion even though there may be a positive adrenal response to *SU* 4885. In such cases the inhibition of the 11β-hydroxylase may still be present, and if one were to measure this inhibition more directly, it might be possible to determine whether there is a response to *SU* 4885 when the change in total 17,21-dihydroxy-20 ketosteroids is not marked. Where total corticosteroid excretion fails to rise, this may be due to failure of the *SU* 4885 to penetrate the adrenocortical cells, or to produce inhibition once it is there. An examination of the values of the 11 oxygenated steroids may present information on this point.

Evaluation of the action of *SU* 4885 should take into consideration the 11-oxy steroids as well as the 11-deoxy steroids. It is possible to separate 11-oxy from 11-deoxy 17-ketosteroids by employing column chromatography on alumina[5]. By means of the ketogenic reaction[6] the 17-OH-corticosteroids may be converted to 17-ketosteroids. These 17-ketosteroids may then be separated into the 11-oxy and 11-deoxy groups and each determined quantitatively by the Zimmermann reaction. The preformed 17-ketosteroids present in the urine are first reduced to alcohols by means of sodium borohydride in order to eliminate them from measurement. We have been utilizing the chromatographic method for the separation of 11-oxy ketosteroids from 11-deoxy ketosteroids and have combined this with the ketogenic reaction to study the effect of *SU* 4885 on human beings.

By expressing the results as the ratio of 11-deoxy : 11-oxy 17-ketogenic steroids, one has a more sensitive measurement of the action of *SU* 4885 than a measurement of total 17-OH-corticosteroids. Table 1 illustrates this by giving the values obtained for various individuals for the total ketogenic steroids and 11-deoxy : 11-oxy 17-ketogenic steroid ratios. It will be seen that even in cases where there were no marked increases in total ketogenic steroids, there were good-sized increases in the ratios. In case 5, there was a rather marked but unexplainable fall in total ketogenic steroids after the administration of *SU* 4885. There was, however, an increase in the 11-deoxy : 11-oxy 17-ketogenic steroid ratio. This technique of measuring the change in ratio may be a

Table 1. Effect of *SU* 4885 on Total 17-Ketogenic Steroids (KGS) and 11-Deoxy : 11-oxy 17-Ketogenic Steroid (KGS) Excretion in Urine

Patient	Control before *SU* 4885		After *SU* 4885‡	
	KGS (mgm./24 hr.)	11-Deoxy-KGS / 11-Oxy-KGS	KGS (mgm./24 hr.)	11-Deoxy-KGS / 11-Oxy-KGS
1	7·1	1·6	15·8, 18·1	2·3, 4·4
2	10·6	1·4	27, 40	2·8, 3·9
3	9·6	1·5	11·9	2·7
4	15·5, 11·8	1·5, 1·7	14·2, 16·8	2·5, 2·4
	12·1	2·0		
5	29, 21	1·9, 2·4	8·5, 9·2	4·1, 4·2
	15·7	2·3		
6*	25	2·5	35, 45, 49	3·5, 2·8, 3·3
7†	4·3	1·0	2·9, 1·9, 2·1	1·5, 1·0, 1·9

Patients 1–5 were adult males who were hospitalized for non-endocrine disorders.
* This patient was a case of hyperadrenalism, possibly tumour.
† This patient was a case of hypopituitarism.
‡ *SU* 4885 was administered orally 6 × 0·5 gm. daily.

relatively simple method for evaluating the action of *SU* 4885 where interpretation of results from determination of total corticosteroids may be ambiguous.

Recently, Butt *et al.*[7] have reported on a similar fractionation technique to investigate the effect of *SU* 4885. They utilized silica-gel chromatography to effect separation of the ketosteroids. Our results support the claim of Butt *et al.*[7] that the 'fractionation' method has greater sensitivity than the total 17-ketogenic steroid method.

We acknowledge the generosity of Ciba Pharmaceutical Products, Inc., Summit, New Jersey, for supplying the *SU* 4885.

The material for this work was made available from patients under the direction of Dr. Donald W. Petit and Dr. Colin Cooper at Los Angeles County General Hospital.

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The Metabolic State of Thiosulphate

Our earlier experimental work using labelled thiosulphate has shown that the two atoms of sulphur in this compound have different fates in the course of metabolism in the animal organism[1]. In rats, the inner sulphur atom is eliminated very quickly from the organism in the form of sulphate, while the outer atom is transformed into the sulphate much more slowly, going probably through a number of intermediate stages. The results of our investigations have shown that the thiosulphate may be the metabolic precursor of the sulphate, and that, however small its concentration in rat urine may be, the endogenous pool of thiosulphate is large (ref. 1*b*).

In the work reported here, rats were injected subcutaneously with 0·8 mgm. of D,L-cystine labelled with sulphur-35 dissolved in 0·5 per cent sodium carbonate, and at the same time with 200 mgm. non-radioactive sodium thiosulphate ($Na_2S_2O_3.5H_2O$). The dose of thiosulphate was repeated after 24 hr. The urine was collected quantitatively at set intervals of time. As a control, we used rats to which radioactive cystine had been given without the simultaneous administration of thiosulphate. The thiosulphate excreted in the collected urine was separated and estimated quantitatively by the method of Gast *et al.*[2], the residual sulphate was removed by adding barium chloride, and the remaining sulphur compounds which were neither thiosulphate nor inorganic sulphate were treated as residual sulphur. The total activity of a given sample of urine, the activity of the thiosulphate, and that of residual sulphur were determined. The activity of the inorganic sulphate was calculated indirectly from the difference.

Table 1. Activities of Excreted Thiosulphate, Sulphate and Residual Sulphur
Results are expressed as a percentage of total activity of urine, after injection of 0·8 mgm. of cystine-^{35}S (4 animals)

Time (hr.)	Activity of thiosulphate		Activity of sulphate		Activity of residual sulphur	
	Range	Average	Range	Average	Range	Average
0–6	1·79–2·28	2·1	46·5–78·5	71·8	19·3–31·4	26·0
6–24	1·88–3·22	2·47	53·7–77	67·4	20·7–44·5	30·1
24–48	2·45–3·60	2·64	51·2–68·8	62·6	28·1–45·5	34·2
48–72	1·69–2·71	2·36	53–72	60·8	26·4–43·5	36·5

Table 2. Activities of Excreted Thiosulphate, Sulphate and Residual Sulphur
Results are expressed as a percentage of total activity of urine, after injection of 0·8 mgm. cystine-^{35}S and 200 mgm. $Na_2S_2O_3.5H_2O$. The dose of $Na_2S_2O_3.5H_2O$ was repeated after 24 hr. (6 animals)

Time (hr.)	Activity of thiosulphate		Activity of sulphate		Activity of residual sulphur	
	Range	Average	Range	Average	Range	Average
0–6	38·5–53·2	43·6	31·7–51·8	44	12·0–15·0	13·5
6–24	1·9–19·5	7·6	56·7–77·0	65·5	21·2–30·0	25·4
0–24	29–41	33	47–52	49	12–19	18
24–48	10·2–30·9	18·95	30·0–60·4	51	19·7–39·2	28
48–72	2·5–7·3	5·3	42·5–57·7	52	37·0–52·5	42·2

Table 1 shows the proportion of radioactivity of the different fractions of sulphur in urine after giving rats cystine alone. Table 2 similarly illustrates the results of experiments when both radioactive cystine and non-radioactive thiosulphate were injected.

As may be seen from Tables 1 and 2 only an insignificant percentage of activity is excreted in the form of thiosulphate after the injection of labelled cystine without the addition of thiosulphate. On the other hand, if at the same time a massive dose of unlabelled thiosulphate is given, 33 per cent of the sulphur produced by the metabolism of cystine is excreted in the urine in the form of thiosulphate in the course of 24 hr. Even after the next 48 hr., considerable quantities of radioactive thiosulphate are excreted when additional thiosulphate has been injected.

Our explanation of these facts is that external introduction of a large dose of thiosulphate inhibits the oxidation of the endogenic thiosulphate. We assume that thiosulphate given from an external source mixes with the pool of endogenous thiosulphate, and in consequence both the excretion and the oxidation of the endogenous thiosulphate take place at the same rate as that of the thiosulphate administered from an external source. A scheme of the relation between the exogenous and endogenous thiosulphate is given in Fig. 1, where $^*A_0$ is the sulphur of the endogenous thiosulphate; $^*A$ is the sulphur of the endogenous thiosulphate excreted in the urine in the form of thiosulphate; $^*B$ is the sulphur in the

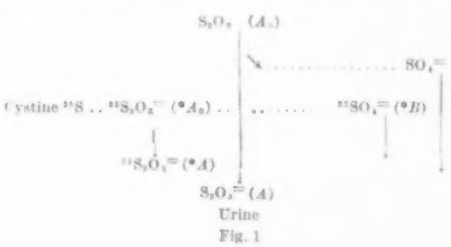

Fig. 1

sulphates originating from the radioactive cystine excreted in urine; A_0 is the sulphur of the injected thiosulphate; A is the sulphur of the injected thiosulphate excreted in the urine in the form of thiosulphate; B is the sulphur in the sulphates originating from the injected thiosulphate excreted in urine.

Quantitatively, if the endogenous and exogenous thiosulphate behave in an identical manner, the following relation would be valid: $^*A_0/^*A = A_0/A$.

We had previously estimated[1] that under normal conditions the rat excretes 0·05–0·1 mgm. of sulphur in the form of the thiosulphate and about 3 mgm. of sulphate sulphur during 24 hr.; that is, the ratio of these two kinds of sulphur may be expressed numerically as 0·01–0·03. The same relation exists between activity of thiosulphate and sulphate after injection of labelled cystine alone (Table 1). After injecting rats with labelled thiosulphate, we showed that the relation of excreted thiosulphate sulphur to the sulphate sulphur (A/B) is given by the average values 0·61, 0·19 and 0·53 for periods 0–6, 6–24 and 0–24 hr. respectively.

If we assume that thiosulphate is the normal precursor of the sulphate and that the small quantity in the urine is only the result of its rapid oxidation in the animal organism, after the injection of thiosulphate the ratio of the sulphur of the endogenous thiosulphate to the sulphur of the endogenous sulphate should be approximately the same as that of the introduced thiosulphate sulphur to the sulphate originating from this: $^*A/^*B = A/B$. Taking the figures from Table 2, we obtain the following values of $^*A/^*B$: 0·99, 0·11, 0·67 for periods 0–6, 6–24 and 0–24 hr. respectively.

The figures obtained for $^*A/^*B$ as compared with values of A/B lie in the range of experimental deviation and these results indicate with great probability that the endogenous thiosulphate behaves like the exogenous, and hence it is the fundamental precursor of the sulphate originating in the organism of the rat.

A full description of the experiments and calculations will be given elsewhere.

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Polysaccharides of *Mycobacterium phlei*

Investigations of the polysaccharides of *Mycobacterium phlei* have been few and mainly concerned with those secreted into the culture medium. Thus Masucci and McAlpine[1] found that a polysaccharide which they isolated from culture filtrates contained D-mannose and D-arabinose. Tennent and Watson[2] isolated a similar product and showed that the molecular weight was 7,300. In the present investigation the intracellular polysaccharides of *M. phlei* were studied.

The organisms were grown on a culture medium (10 litres) consisting of 'Oxoid' bacteriological peptone, 1 per cent; 'Lab. Lemco', 1 per cent; sodium chloride, 0·5 per cent, and glycerol, 5 per cent at 37° for 16 days. The cells were separated from the medium, washed with 0·14 *M* sodium chloride, suspended in phosphate buffer, *p*H 8, and disintegrated in batches of 250 ml. by shaking at 0° for 5 hr. with ballotini glass balls (1 mm. diameter) in a vibratory ball mill. The suspension of broken cells was diluted to 1 litre with phosphate buffer, *p*H 8, and then adjusted to *p*H 4 with dilute acetic acid. The suspension was centrifuged at 2,600 r.p.m. at 0° and the precipitate (cell debris, nucleoproteins, etc.) discarded. The supernatant liquids from the various batches were combined, concentrated to 1 litre by freeze-drying and then mixed with 5 volumes of ethanol. The precipitate so produced was centrifuged off, dissolved in distilled water, dialysed and freeze-dried to give a crude polysaccharide fraction (12 gm.). $[\alpha]_D^{20} + 164°$; N, 0·6 per cent; P, 0·2 per cent. Examination of acidic hydrolysates showed the presence of glucose and small amounts of mannose and arabinose. The presence of glycogen was indicated by the formation of a brown colour with iodine.

The crude polysaccharide (5·9 gm.) was fractionated further by the use of cetrimide ('Cetavlon', Imperial Chemical Industries Pharmaceuticals, Ltd.) in the presence of borate[3]. Four fractions were obtained: fraction I (30 mgm.) was precipitated at *p*H 7·5, and, after acid hydrolysis, contained arabinose, glucose, mannose and amino-acids; fraction II (4·5 gm.) was precipitated at *p*H 9·5 and contained only glucose; fraction III (40 mgm.) was precipitated at *p*H 10 and contained glucose and a trace of mannose, and fraction IV (0·6 gm.) did not precipitate with cetrimide–borate and contained mainly arabinose, a smaller amount of mannose, some glucose and a trace of ribose. Fraction IV was isolated by dialysing the supernatant liquid, freeze-drying and extracting the dry solid with chloroform to remove the cetrimide.

The major fraction (fraction II) was glycogen as shown by the infra-red spectrum (peaks at 930, 845 and 758 cm.$^{-1}$), which was identical with that of an authentic sample of liver glycogen examined at the same time[4], and by the production of a brown colour with iodine. The absorption curve of the iodine complex had $\lambda_{max.}$ 390 mμ. This was lower than that of other glycogens[5], for example, *Mytelus edulis*, 420 mμ, rabbit liver, 490 mμ, and *Bacillus megaterium*, 520 mμ. The intensity of absorption was also lower (E_{390} 0·27 with 0·1 per cent glycogen in 0·01 per cent iodine and 0·2 per cent potassium iodide). The $\lambda_{max.}$ was somewhat variable; another sample had $\lambda_{max.}$ 405 mμ. The glycogen fraction was homogeneous when examined by boundary electrophoresis in borate buffer *p*H 9·2. The polysaccharide also migrated towards the anode in veronal buffer *p*H 9·2, but much more slowly than in borate. This may have been due to the presence of a small number of phosphate groups (phosphorus content, 0·03 per cent).

The second major fraction (fraction IV) contained 3 per cent nitrogen, which was due to the presence of protein and a small amount of nucleic acid; no amino-sugars could be detected. The fraction was heterogeneous when examined by boundary electrophoresis, containing at least two components when examined in borate, *p*H 9·2, glycine, *p*H 9·8, and veronal, *p*H 8·6. The migration in the glycine and veronal buffers could be due to the presence of protein in the fraction. Attempts to remove the protein by precipitation with trichloroacetic acid or by denatura-

tion by shaking with chloroform–octanol (9 : 1) were unsuccessful and resulted in the production of fractions containing different proportions of protein. These results indicated that fraction IV was a mixture of polysaccharide–protein complexes.

When the organisms were grown on a medium which contained 0·4 per cent ammonium lactate instead of 5 per cent glycerol, no glycogen could be isolated from the cells, the polysaccharide being essentially similar to fraction IV. The organisms isolated after growth in 90 litres of a medium containing 'Oxoid' bacteriological peptone 1 per cent, 'Lab. Lemco' 0·5 per cent, sodium chloride 0·5 per cent and ammonium lactate 0·4 per cent for 16 days at 37° were washed free from medium and disintegrated by shaking with ballotini glass balls at 0°. The broken cells were extracted at *p*H 8, and the suspension then adjusted to *p*H 4, centrifuged at 2,600 r.p.m., and the supernatant liquid decanted. The process of extraction at *p*H 8 and reprecipitation at *p*H 4 was repeated twice on the precipitate and the three supernatant liquids were combined and treated with 3 vol. of ethanol. This material contained a considerable amount of nucleic acid which was then removed by precipitation as the lanthanum salt. The resulting polysaccharide (1·74 gm.) isolated from the non-precipitable fraction was similar to fraction IV described above in containing protein (nitrogen content, 5·2 per cent) which could not be easily removed and in being electrophoretically inhomogeneous. No glycogen could be detected by means of iodine.

This material (fraction V ; 1·7 gm.) was further separated into two components by precipitation with 50 per cent ethanol in the presence of 0·01 *M* zinc sulphate. The precipitate (fraction V*a* ; 790 mgm.) still contained protein (N, 5·0 per cent), and paper chromatographic examination of acid hydrolysates showed that mannose and glucose were present in a proportion of 5 : 1 and that arabinose was absent. The supernatant fraction also contained protein, and acid hydrolysates contained arabinose and a little mannose. This fraction was not investigated further.

Fraction V*a* had $[\alpha]_D^{20} + 20°$ in water and an infra-red spectrum which showed peaks at 975, 905, 880 and 810 cm.$^{-1}$. Further purification was carried out by the use of Fehling's solution, which is known to precipitate mannans[6]. The precipitate so produced was dissolved in dilute acid, dialysed and freeze-dried. This purified product (30 per cent by weight of fraction V*a*) contained mannose and glucose (5 : 1) and 0·96 per cent nitrogen. A positive optical rotation ($[\alpha]_D^{20} + 67°$ in water) indicated that it was probably an α-glucomannan. Examination in the ultracentrifuge (kindly carried out by Dr. D. R. Stanworth) showed the presence of three components ; one was a minor one (10 per cent) and the other two were only partly resolved even after prolonged centrifuging at 60,000 r.p.m. The infra-red spectrum in the region 1,000–800 cm.$^{-1}$ was similar to that of fraction V*a*. The spectrum had some similarities with that of a sample of yeast α-mannan (peaks at 975, 917, 885 and 813 cm.$^{-1}$) and with that of α-glucomannan II isolated from yeast cell walls by Kessler and Nickerson's method[7] (peaks at 980, 915, 890 and 815 cm.$^{-1}$) but they were not identical.

It can be concluded, therefore, that at least three intracellular polysaccharides are produced by *M. phlei*, a glycogen, an α-glucomannan and a polysaccharide containing mainly arabinose.

We thank Prof. M. Stacey for his interest and Mr. E. T. J. Chelton and Mr. C. G. James for technical assistance. Thanks are also due to the Medical Research Council for financial assistance. We are also grateful for the award to one of us (M. N.) of a scholarship under the Colombo Plan.

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Distribution of Cholinesterase within the Kidney of the Domestic Fowl

During investigations in this laboratory it was noticed that the distribution of cholinesterase within the fowl kidney was not uniform. The following observations are recorded in view of the sparse information regarding cholinesterases in the bird. The nomenclature of Augustinsson and Nachmansohn[1] is used throughout.

Males and females 12–14 weeks old were killed by an overdose of nembutal, the kidneys excised and frozen sections cut at 50μ and stained for true cholinesterase[2]. It was also possible to obtain paraffin sections by slightly modifying the technique ; slices 1 mm. thick were cut from the kidney and left in the substrate for 18 hr. at 37° C. The subsequent treatment was as given by Coupland and Holmes[3]. The tissue was then embedded in paraffin and sectioned in the normal way. With this procedure the very heavy deposit on the surface of the block tended to obscure a certain amount of detail, but thin sections were obtained and gave the same results as the frozen sections. In both methods pseudocholinesterase was also demonstrated by substituting butyrothiocholine iodide as substrate, and controls were obtained by preliminary incubation of the sections in 1×10^{-7} di-*iso*propylfluorophosphonate[3]. No distinction could be made between kidneys obtained from males and females.

The distribution of both true and pseudocholinesterase appeared to be very similar, but the degree of staining for the two enzymes differed considerably. Both were found in quantity in the vascular system, although this would be expected since it has been shown that cholinesterase, either the pseudo-enzyme or a mixture of true and pseudocholinesterase, is present in avian plasma[4]. The ureter wall stained very heavily for both enzymes (Fig. 1), but the tubule walls appeared to be free (Fig. 2). No cholinesterases were found in the contents of the lumen of tubules or ureters (Figs. 1, 2). Perhaps of greater importance was the heavy staining of the Bowman's capsule, particularly for true cholinesterase (Fig. 2), and this may be related to the presence of these enzymes in avian plasma. However, neither enzyme was found in the tubule or uretal contents, which suggested that

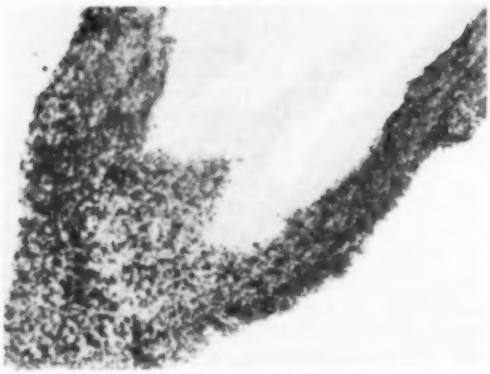

Fig. 1. Ureter. Localization of true cholinesterase only in the wall of the ureter. Frozen section

Fig. 2. Kidney section showing true cholinesterase activity in Bowman's capsule. The tubule wall and contents have not taken the stain. Paraffin section

they are not being excreted except in amounts very much lower than in plasma or in changed form.

It has been suggested that cholinesterase is involved in the sodium pump mechanism[5], and it is therefore possible that the presence of these enzymes in Bowman's capsule is related to kidney function. This suggestion must remain speculative until more is known about the physiological significance of these enzymes.

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Hæmolytic Activity of Colloidal Silica

Colloidal silica is highly toxic when administered parenterally[1,2]. In isolated biological systems silica has been shown to interfere with some enzymes[3,4], activate blood clotting and pharmacologically active substances in plasma[2] and interfere with the red cell envelope[6]. Most of these effects are probably due to the adsorption and partial denaturation of proteins at the surface of silica particles[5,7].

The ultimate particle size of the colloid varies with the conditions of preparation and storage. Most of the investigators quoted have observed that aged sols have far greater biological effects than freshly prepared silicic acid solutions[2–6]. The difference is presumably due to the spontaneous growth of the particles on ageing. Using modern methods it is now possible to make silica dispersions of almost any desired particle size and thus evaluate quantitatively the differences between their biological activity. Such observations have been reported by one of us in relation to clotting of blood[2]. In the present work we have studied the effects of various types of colloidal silica on intact red cells.

To obtain silicic acid, 1–5 per cent solutions of sodium silicate were passed through a column of cation exchange resin ('Zeo-Karb 225'). According to the concentration, *p*H and subsequent heating of the material, a series of sols of particle size from 2 mμ to 6mμ were obtained (cf. Iler[8]). In addition we used commercial preparations of silica ('Ludox *SM*', Du Pont: 7 mμ and 'Syton *W*20', Monsanto: about 30 mμ).

Human red cells were washed three times with buffered isotonic saline (phosphate or bicarbonate buffer, *p*H 7·4) and suspended in saline. One-tenth volumes of serial dilutions of silica were then added to a series of tubes with the red cell suspensions and the contents were incubated at 37° C. with occasional gentle agitation. After centrifuging, the supernatant haemoglobin was measured and expressed as a percentage of the total.

Fig. 1 shows the result of a typical experiment with a 2 per cent cell suspension incubated with silica for 30 min. It is obvious that colloidal silica can be a very potent hæmolytic agent. For example, 1 μgm./ml. of the 30-mμ particles lyses about 50 per cent of the cells. Since the surface area of this silica is somewhat less than 1 cm.²/μgm. while that of 2 per cent cell suspension is about 150 cm.²/ml., it follows that contact of silica with a very small portion of the red cell surface is sufficient to produce hæmolysis. The hæmolytic activity decreases with the particle size

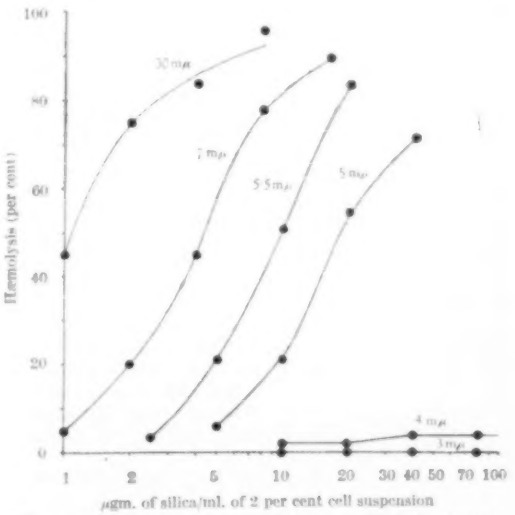

Fig. 1. Hæmolysis of 2 per cent red cell suspension incubated with colloidal silica for 30 min. at 37° C. The figures above the curves indicate the mean particle diameter of the colloid

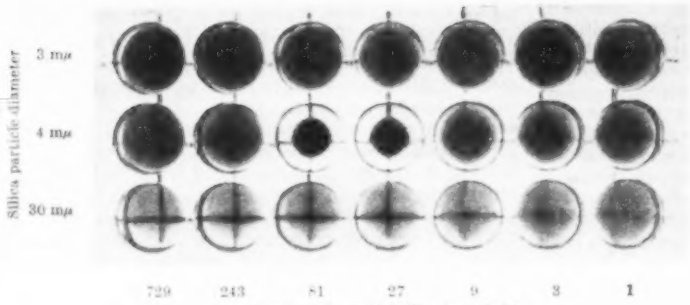

Fig. 2. Hæmagglutination plate viewed from above. 2 per cent red cell suspension was incubated with colloidal silica. Black lines were drawn on the reverse side to emphasize the transparency of the hæmolysed samples. Top row, no visible change; second row, zonal agglutination; bottom row, hæmolysis

of the colloid until it becomes negligible at about 4 mμ diameter. We have also observed that particles in the range of 3·5–7 mμ have a powerful agglutinating effect on the red cells, with a well-marked prozone (Fig. 2). Silica of 3-mμ or smaller particle size has no such activity but protects the cells against the agglutination and hæmolysis by the larger particles. This 'blocking' effect occurs only when the smaller particles are introduced into the cell suspension before the larger ones and it persists after repeated washing with saline, which probably indicates an irreversible adsorption of silica on to the erythrocyte surface. Such 'coated' red cells have other properties in addition to their resistance to the larger particles of silica. Thus they are not hæmolysed by streptolysin *O* and the saponin fragility is somewhat decreased. On the other hand, these cells become more susceptible to immune (rat) hæmolysins and to primaquine. The osmotic fragility is not altered, nor is there any obvious abnormality in appearance except that the cells do not become spherocytic when examined between glass slides and coverslips as do normal washed erythrocytes[10].

In all these experiments it is essential to use well-washed cells because even small traces of plasma markedly inhibit the action of silica. The addition of 1 : 200 plasma to the system as in Fig. 1 completely prevents hæmolysis. The plasma must, however, come in contact with silica before the latter is adsorbed by the red cells. Even a few seconds delay suffices to abolish the protective effect of the plasma. This phenomenon is evidently due to the coating of the silica by certain plasma components. The substances in question are non-dialysable and can be recovered in alkaline eluates from powdered silica which has been exposed to plasma or serum. Such eluates retain their activity after heating to 100° C.

Our observations on the agglutinating and blocking activity of silica agree with the qualitative findings of Renton and Hancock[6], who suggested that these effects may be analogous to those of agglutinating and incomplete antibodies, respectively. The present results extend this model to cover hæmolysis as well.

Although our present knowledge of the red cell structure is still fragmentary, the reaction between silica and the cell membrane may be visualized in general terms as a two-stage process: first, a rapid adsorption of the particles by the cell surface, due mainly to the ionic attraction between silica and the amino-groups at the cell surface and further reinforced by hydrogen bonds and van der Waals forces[7]; secondly, protein denaturation, the extent of which may depend purely on the geometrical relation between the colloidal particles and the protein molecules, as was previously suggested in connexion with blood clotting[5,8]. Individual silica particles of less than 3·5 mμ may not provide sufficient contiguous surface to permit significant unfolding of the much larger protein molecules. Contact with larger particles will, however, allow such unfolding (denaturation), and the resulting interference with the integrity of the cell membrane then leads to agglutination or hæmolysis according to the degree of denaturation. The geometrical picture may, of course, be oversimplified and other physical differences between the large and the small colloidal units may be contributory factors[11]. Despite these reservations, colloidal silica may prove a useful tool in the elucidation of the red cell structure.

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PHYSIOLOGY

The Psychotomimetic Properties of 3,4,5-Trimethoxyamphetamine

dl-3,4,5-Trimethoxyamphetamine (*dl*-TMA), first prepared as a homologue of mescaline in 1947[1], has remained to a large measure unexplored. A single paper has described its effects in human subjects[2], demonstrating that the drug allows stroboscope-induced hallucinations at the levels employed, namely, 0·8–2·0 mgm./kgm., orally. In the present work, *dl*-3,4,5-trimethoxyamphetamine was synthesized by the general method of Ramirez and Burger[3] and was chemically identical to that previously described[1]. Pharmacological similarity was demonstrated by the administration of between 1·6 and 2·0 mgm./kgm. as the hydrochloride, to three adult male subjects. The responses were found to be parallel in intensity and duration to those described earlier[2], although the vivid hallucinations reported were not observed.

It has been found, however, that with an increased dosage of the drug, the psychotropic response changed in a most dramatic manner. Dosages of 2·8–3·5 mgm./kgm. were given to five adult male subjects, all of whom had had previous experience with either mescaline or lysergic acid diethylamide.

The physical changes observed were similar for all subjects employed. In each case, after about half an hour, there ensued a period of autonomic distress, characterized by sweating, tremor, and chills as well as nausea and dizziness. This phase lasted no more than an hour. The slight but definite systolic blood pressure increase of about 10 mm. mercury returned to normal at the end of this phase. The concurrent diastolic increase was barely perceptible (*c.* 2 mm. mercury). During the remainder of each experiment (approximately another 6–8 hr., which includes the period of extreme mental derangement described below) very few overt physical signs of drug effect were evident. Pupillary dilatation and slight motor inco-ordination were noted. Pulse increase was negligible.

The psychic changes observed, however, were extreme and showed considerable individual variability. The initial effects, at about 2 hr. from the ingestion of the drug, were mescaline-like, involving intensification of visual experience, including amplification and distortion of colour, texture, form, and spatial relationships. These effects were distinctly less than those expected from a pharmacologically equivalent dose (2×) of mescaline. Auditory and tactile sensations were also intensified, and both paraesthesia and synaesthesia were noted on occasion. None of the subjects displayed the enhanced capacity for empathy characteristic of mescaline.

The emotional responses elicited during the period of maximum *dl*-3,4,5-trimethoxyamphetamine intoxication (3–5 hr. from the start of the experiment) were striking in their intensity. Anger, hostility, and megalomaniac euphoria dominated the subject's thoughts and conversation. Actual acts of hostility were not observed, but it was felt that, in at least two subjects, provocation would have precipitated homicidal violence. All subjects reported imagery, either patterned or scenic, with eyes closed. Recollection of past experiences did not seem to be enhanced, and intellectual performance appeared to be somewhat impaired. Once the plateau of intoxication had passed, return to normal was rapid. The subjects experienced no clouding of consciousness, and subsequent recall of events was excellent.

Due to the unexpectedly anti-social character of the response to larger doses of the drug (a response unobserved in more than 40 mescaline subjects), a warning concerning adequate supervision during experimentation with this new drug seems desirable.

Investigations employing the optical isomers, as well as structural homologues, of *dl*-3,4,5-trimethoxyamphetamine are in progress.

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The Conversion Ratio as a Discriminatory Test for Thyroid Activity in Fish

The rate of conversion of administered inorganic radioiodine into protein-bound radioiodine of the plasma has been used frequently to evaluate thyroid activity in mammals. The test is recognized as having good discriminatory power in higher vertebrates[1,2], but the relatively large sample of blood required for separation of serum by the usual methods has made the test impractical for small fish. A method is described here for determining protein-bound radioiodine as an *in vivo* test in fish of 30 gm. or more and as a terminal test in fish as small as 1 gm.

Each fish received an intraperitoneal injection of carrier-free iodine-131, the dosage depending on the weight of the fish and the detection instrument used. When using a scintillation well-counter, the instrument of choice, 0·1 μc. iodine-131 per gm. body-weight was sufficient. Blood sampling for *in vivo* determinations in anæsthetized trout were carried out by direct cardiac puncture with a ¼ c.c. heparinized syringe. Blood was transferred to a heparinized capillary tube and the vacant end of the tube plugged with 'Plasticene' or sealed with a small concentrated flame such as that of a propane torch. Blood may be obtained from very small fish by cutting off the tail and collecting the blood as it flows from the caudal artery into a heparinized capillary tube. Sealed tubes were centrifuged in a hæmatocrit centrifuge or in a 15-ml. bucket centrifuge fitted with hollow wooden adapters for the tubes. After separation of the cells, the tubes were scratched and broken between cells and plasma and the plasma was expressed into a 15-ml. centrifuge tube containing 2 ml. of 20 per cent trichloroacetic acid. The protein precipitate was stirred vigorously with a glass rod and centrifuged down. The supernatant containing the inorganic iodine-131 was decanted and saved. The precipitate was washed three times with 2-ml. portions of 2·5 per cent trichloroacetic acid, each time breaking up and stirring the precipitate and then centrifuging. All trichloroacetic acid washes, totalling 8 ml., were combined and saved. The precipitate was then dissolved in sodium hydroxide and diluted to the same volume as the combined supernatant washings. Finally, the radioactivity of both fractions was counted. Using the well-crystal scintillation counter, aliquots of supernatant and dissolved precipitate were pipetted into counter tubes and counted to 10,000 counts. An end-probe scintillation counter was occasionally used, and greatest sensitivity was achieved by securing the probe with crystal facing up in a lead castle and placing the fractions contained in a small beaker directly on the crystal. After subtraction of the background count, percentage of protein-bound iodine-131 is calculated as :

$$\frac{\text{Prot.-bound iodine-131 in counts per min. (precip.)}}{\text{Prot.-bound iodine-131 + iodine-131 (combined counts of precip. and supernat.)}} \times 100$$

Serial determinations in rainbow trout (*Salmo gairdneri*) and starry flounder (*Platichthys stellatus*) have shown that protein-bound radiothyroxine in the plasma gradually increases relative to inorganic radioiodide until approximately the fourth or fifth day, after which it begins to fall. The rate of increase usually is most rapid just before the inflexion and represents the period when the greatest percentage

Table 1. Comparison of Thyroid Radioiodide Uptakes and Conversion Ratios in Normal and Thiourea-treated Flounder

Controls		Thiourea-treated	
4-day uptake	4-day conversion ratio	4-day uptake	4-day conversion ratio
6·40	14·3	2·05	1·10
2·23	18·3	2·80	0·22
5·08	10·9	5·60	0·19
6·90	16·0	2·16	0·07
8·90	13·8	2·93	0·54
		2·05	0·42

of labelled thyroxine molecules is secreted from the thyroid gland. When breakdown or excretion of radiothyroxine exceeds its rate of appearance in the blood, the conversion ratio falls.

Usually only one determination is made at a fixed interval of time after the injection of radioiodide. Sampling should be made before the maximum value for protein-bound iodine-131 is reached, and the ideal time to sample will vary with the species and with the experimental conditions. In general, the more active the thyroid gland, the earlier the ideal sampling time will be. A 4-day interval between administration of the tracer dose and sampling has been found satisfactory for rainbow trout and starry flounder under normal conditions. Periods longer than 4 days rarely prove worth while, because the reliability of the method is rapidly limited by loss of radioiodide through excretion and physical decay.

In Table 1 the 4-day conversion ratios and the 4-day thyroid radioiodide uptakes of normal starry flounder and flounder immersed 11 days in 0·04 per cent thiourea are compared. In this experiment, the 4-day conversion ratio is of far greater value than thyroid radioiodide uptake for determining the degree of thyroid inhibition achieved. The conversion ratios average 14·6 for the normal flounder as compared with 0·42 in those flounders treated with thiourea; this shows that blockage of hormone synthesis is essentially complete. Thyroid radioiodide uptake is comparatively useless for such a test, because some radioiodide is accumulated by the inhibited gland.

It is desirable to reduce the time-interval before sampling if the experimental treatment is expected to stimulate thyroid activity greatly. Table 2 shows the 2-day conversion ratios of starry flounder treated with thyroid-stimulating hormone. Two injections of the hormone were given, one three days and the other six days before the injection of radioiodide for the determination of protein-bound iodine-131.

In spite of the small size of sample, the relative effectiveness of the different dosages of thyroid-stimulating hormone is easily estimated.

Many factors influence the conversion ratio, making its mathematical analysis exceedingly complex[3].

Table 2. Effect of Thyroid-Stimulating Hormone on the 2-day Conversion Ratio of Starry Flounder (*Platichthys stellatus*) Experimental temperature, 14·0° C.; experimental salinity, 26 per mille

Controls		Treated with thyroid-stimulating hormone 0·0001 U.S.P. units/gm.		0·001 U.S.P. units/gm.		0·01 U.S.P. units/gm.	
Body-weight	2-day conversion ratio	Body-weight	2-day conversion ratio	Body-weight	2-day conversion ratio	Body-weight	2-day conversion ratio
126·5	1·96	97·0	4·5	84	39·7	79·5	38·0
93·5	1·25	93·5	2·0	77·5	13·8	76	46·3
81·0	1·94	71·5	13·7	75	22·6	68·5	37·2
av. 1·72		av. 6·7		av. 25·4		av. 40·5	

However, for purposes of distinguishing different levels of thyroid activity, the test is accurate, simple to perform and possesses greater discriminatory power than the uptake of radioiodide by the thyroid gland. It has the important advantage of measuring the relative rate of secretion of thyroid hormone rather than the more indirect iodide-trapping activity of the thyroid gland. The test should prove particularly valuable in assessing thyroid activity of very small fish.

Thyroid-stimulating hormone was kindly supplied by Wayne Donaldson, of Parke, Davis and Company, Detroit. Financial assistance was received through grant *G*-8502 of the National Science Foundation, Washington, D.C., awarded to W. S. Hoar, University of British Columbia.

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Transport of Phosphate into the Erythrocyte

The active transport of inorganic phosphate into the red blood cell is generally believed to be closely related to glycolysis, although the actual mechanism of transfer is unknown[1]. Gourley[2] considered that phosphate enters the erythrocyte through the formation of adenosine triphosphate at the cell surface. Prankerd *et al.*[3] and Bartlett[4] concluded from their investigations that inorganic phosphate is transferred into the cell by incorporation into 1,3-diphosphoglyceric acid. Our own experimental evidence suggests that the transfer of inorganic phosphate is independent of glycolysis.

Whole blood was incubated at 37° C. with orthophosphate labelled with phosphorus-32. The disappearance of phosphorus-32 from the plasma was measured over a 2-hr. period and calculated on the basis of a 40 per cent haematocrit. In a series of eight samples the rate of disappearance of phosphorus-32 in the presence of glucose (200 mgm. per cent) was 29·3 per cent/hr. ± 3·1 per cent. When iodoacetic acid was included in the incubation mixture to a final concentration of 10^{-3} molar, lactic acid production was completely inhibited, and phosphorus-32 left the plasma in nine samples at a mean rate of 12·5 per cent/hr. ± 1·1 per cent. Eight samples of whole blood incubated with glucose, iodoacetic acid and adenosine (6·25 m.mol./l.) were found to show a rate of disappearance of plasma phosphorus-32 similar to those samples incubated with glucose alone (29·8 per cent/hr. ± 3·7 per cent). Under these conditions there was again no production of lactic acid. The similarity of the two rates of influx with glucose alone, and with glucose, iodoacetic acid and adenosine suggests that the mechanism of transfer of phosphate into the cell under these two conditions may be identical. To establish further the similarity of transport in the presence or absence of glycolysis we studied the effects of variation of incubation temperature and of external phosphate concentration on the rate of entry of phosphate into the erythrocyte.

In Fig. 1, it will be noted that as the external phosphate concentration is increased there is an increase in the rate of entry of orthophosphate into the red cell. This increase is identical in the presence of either glucose, or glucose, adenosine and iodoacetic acid. In Fig. 2, the effect of change of temperature is shown. An increase in temperature causes an increase in the transfer-rate constant which is identical under both conditions. These findings indicate that phosphate enters the red blood cells at similar rates whether glycolysis is proceeding or not.

To find out whether the phosphate which entered the cell under these two conditions would be metabolized in a similar fashion the distribution of radioactive phosphorus-32 within red cell phosphate esters was studied by the method of anion exchange column

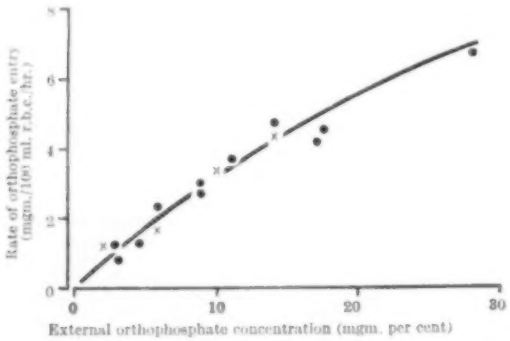

Fig. 1. Effect of variation of external phosphate concentration on the rate of total phosphate entry into the red blood cell. Washed erythrocytes were suspended in veronal acetate buffer (pH 7·45); and incubated for 2 hr. at 37° C. with 0·2 μc. phosphorus-32 sodium phosphate in the presence of: (1) glucose 200 mgm. per cent (●); (2) glucose 200 mgm. per cent, iodoacetic acid 10^{-3} M and adenosine 6·25 mM (×)

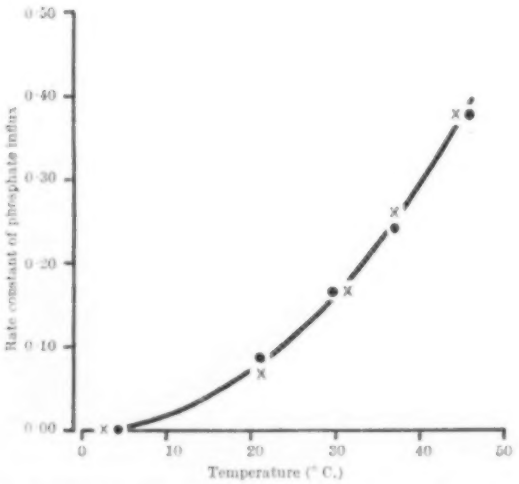

Fig. 2. Effect of variation of incubation temperature on the rate constant of phosphate influx into red blood cells. Washed erythrocytes were suspended in veronal acetate buffer (pH 7·45, inorganic phosphate concentration 3·0 mgm. per cent). These cells were incubated for 2 hr. at 37° C. with 0·2 μc. phosphorus-32 sodium phosphate in the presence of: (1) glucose 200 mgm. per cent (●); (2) glucose 200 mgm. per cent, iodoacetic acid 10^{-3} M and adenosine 6·25 mM (×).
Rate constant of phosphate influx in each experiment was corrected to a hæmatocrit of 40 per cent

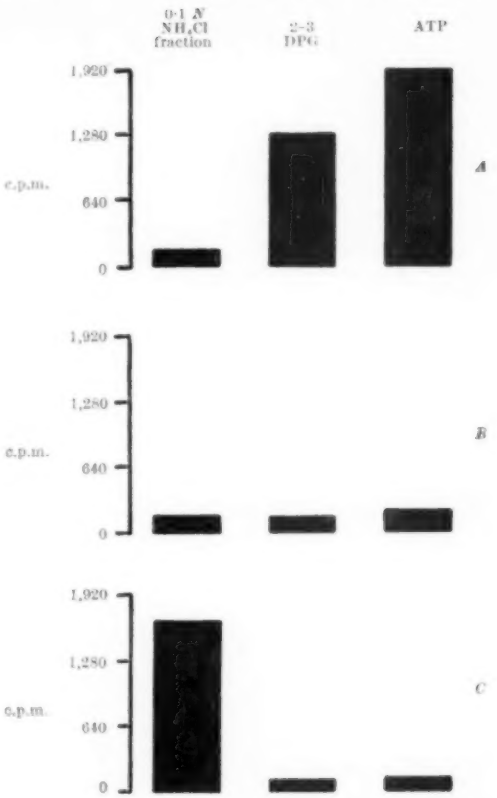

Fig. 3. The radioactivity (c.p.m.) of erythrocyte phosphate esters after 2-hr. incubation at 37° C. (20 ml. of blood with 20 μc. of phosphorus-32) in the presence of: A, glucose (200 mgm. per cent); B, glucose (200 mgm. per cent) and iodoacetic acid 10^{-3} M; C, glucose (200 mgm. per cent), iodoacetic acid 10^{-3} M and adenosine 6·25 mM

chromatography of Bartlett[5]. It may be seen in Fig. 3 that in the presence of glucose most of the phosphorus-32 was found in adenosine triphosphate (ATP) and 2,3-diphosphoglyceric acid (2–3 DPG) (Fig. 3, A). Inhibition of glycolysis by iodoacetic acid (Fig. 3, B) prevented the entry of ^{32}P-orthophosphate into these esters. When adenosine was included radioactivity was found in the 0·1 N ammonium chloride fraction, with very little in adenosine triphosphate (ATP) or 2,3-diphosphoglyceric acid (2–3 DPG) (Fig. 3, C). In A and B the amount of organic phosphate in the 0·1 N ammonium chloride fraction (known to contain hexose diphosphates but no monophosphate[5]) was low. In C, however, this fraction contained greater quantities both of organic phosphate and fructose. Fructose was determined by the Roe modification of the Seliwanoff procedure[6]. In two experiments it was found that the excess phosphate and fructose in C occurred in the ratio of 1·83 moles of phosphorus/mole of fructose. These findings suggested that the radioactivity which appeared in the 0·1 N ammonium chloride fraction under these conditions was in fructose-1,6-diphosphate.

In the presence of glucose alone (Fig. 3, A) orthophosphate is probably esterified by way of the glyceraldehyde-3-phosphate dehydrogenase reaction. With

glucose, iodoacetic acid and adenosine, glycolysis is inhibited and inorganic phosphate is esterified, presumably in the purine nucleoside phosphorylase reaction, to form ribose-1-phosphate. This material can then be metabolized through the hexose monophosphate shunt and result in an accumulation of fructose-1,6-diphosphate[7]. Under these two conditions inorganic phosphate enters the red blood cell at the same rate yet follows different metabolic pathways. The identical kinetics of phosphate transfer, whether glycolysis is active or inhibited, suggests that the limiting step of entry of phosphate into the red blood cell is similar under both conditions and is not dependent on glycolysis.

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Control of Fertility by 6-Azauridine

We have previously suggested that agents known to inhibit cell division might be effective ovicides in mammals, in amounts which are non-toxic to the pregnant female[1]. We have reported on a few such agents, and our results in general supported the hypothesis that it might be possible to separate the effects on the ovum and on the maternal organism[2]. Since that time, we have examined a number of other substances, and in this communication we wish to direct attention to one of these in particular. This substance, 6-azauridine (2-ribofuranosyl-*as*-triazine-3, 5(2*H*,4*H*)-dione) ('AzUR'), is so far the one which most closely approaches our aim of finding an oral agent which might control human pregnancy, with minimal toxic effects.

'AzUR' has been shown to be a highly active inhibitor of the growth of some species of bacteria[3], and of mammalian tumours, both in tissue culture[4,5] and *in vivo*[4,6]. It has also been found to be effective in leukemia in man[7]. It is reported to have very low toxicity in mice[4,6,8] and in man[7,8], though it is somewhat toxic in dogs[4,6].

In our experiments, 'AzUR' was dissolved in water and given to mice by stomach tube in doses related to the weight of the animals. As in our previous work, we used Swiss albino mice. It has been reported that 'AzUR', because of its rapid rate of excretion, is more effective when given in divided doses[4]. In some of our experiments, therefore, we compared the effect of administering the substance in one single dose with that of administering it in three equal fractions of the daily dose at intervals of 8 hr.

Toxicity. The mildest sign of toxicity was a temporary fall in weight, which was rapidly regained when the 'AzUR' was withdrawn. More severe toxic effects were diarrhœa, a staring coat and death.

In non-pregnant animals, we have found that single doses of 0·5 mgm./gm., given for 9 consecutive days, were without effect in mature animals. In weanling animals, the same dose produced a significant but temporary loss in weight. Neither the younger nor the older mice showed any impairment of fertility when they were afterwards mated, and they produced normal litters. Thus, 'AzUR' does not appear to affect unfertilized ova.

In pregnant animals, the occurrence of toxicity depended on the size of the daily dose of 'AzUR', the number of days during which it was given, whether it was given as a single dose or in divided doses, and the stage of pregnancy. A single dose of 4 mgm./gm., given on the fourth day of pregnancy, was without toxic effect. Three consecutive single doses given on the fourth, fifth and sixth days killed some animals at 4 mgm./gm., and caused loss of weight at 1 mgm./gm.

Because of these effects, most of our further work was carried out with doses of 0·5 mgm./gm. Single or divided doses at this level, given for 1–4 days, were non-toxic in the early stages of pregnancy. Given for three consecutive days on or after the tenth day of pregnancy, they led to the death of several of the mothers. We believe that this was secondary to the death of the large conceptus at these late stages of pregnancy (see below).

Effect on pregnancy. The effect on pregnancy, like the toxicity, also depended on the dose, the duration of administration, the state of pregnancy and whether the drug was given in one dose or in divided amounts.

The most regularly effective time of dosing was for three consecutive days from the second, third or fourth day of pregnancy. Thus, in single doses over three days from the fourth to sixth day of pregnancy, 1 mgm./gm. interrupted every pregnancy, whereas 0·5 mgm./gm. interrupted about 50 per cent of pregnancies. Given for four days (third to sixth) instead of three days, single doses of 0·5 mgm./gm. interrupted all pregnancies. In divided doses, however, 0·5 mgm./gm. a day was invariably effective in interrupting pregnancy when given for only three days.

'AzUR' was less effective in the very earliest stages of pregnancy, so that 0·5 mgm./gm. given daily in divided doses for the first three days after copulation interrupted only 9 out of 16 pregnancies. Again, the same dose of 'AzUR' interrupted only half the pregnancies when given from the tenth to twelfth day, and none when given from the fourteenth to sixteenth day. There was, however, an important difference in the litters born to mothers dosed early, or late, in pregnancy. Those born to mothers dosed early in pregnancy survived, and were apparently quite normal; they were able, for example, themselves to conceive and rear their own young. Those born to mothers dosed late in pregnancy were smaller in number, and most of the young died within two days of birth.

The time of termination of pregnancy was related to the dosing schedule. Thus, with single doses over four consecutive days, from the third to the sixth day, pregnancy was terminated between the ninth and fifteenth day with 1 mgm./gm., and between the fourteenth and eighteenth day with 0·5 mgm./gm. Fractional doses totalling 0·5 mgm./gm. daily pro-

duced even earlier termination, between the eighth and the ninth day.

'AzUR' thus appears to have a selective action upon the conceptus during part of its existence. At particular levels, it does not affect the mother. Nor does it exert its maximum ovicidal effect during the very earliest stages of pregnancy, though this may be due to inaccessibility of the ovum rather than to its insensitivity. Again, it gradually ceases to affect the conceptus during the later stages of pregnancy, until eventually it allows the birth of some live young. Nevertheless, the size of litter is reduced, and this, together with the absence of toxicity on the mother at other stages, makes us believe that the apparent toxicity in the late stages of pregnancy are due to the death of one or two foetuses, which by then are quite large.

A great deal more work needs to be done with 'AzUR' before we can decide whether it might be of use in the control of human fertility. There are, however, already several features of the incomplete results so far obtained which provide a considerable incentive to pursue this work. First, at doses which interrupt pregnancy, 'AzUR' has no effect on the unfertilized ovum, nor—with one exception—on the mother. The exception is the ill-effects produced when 'AzUR' is given late in pregnancy. Secondly, young born from mothers which were inadequately dosed seem to be perfectly healthy, and are themselves capable in due course of producing and rearing normal young. This lessens the possibility that, if 'AzUR' were to be used in the control of human fertility, congenital malformations might be produced in young born through inadequate dosing. Thirdly, there is now considerable evidence that 'AzUR' has very low toxicity in man. Amounts equivalent to 0·3 mgm./gm. daily, given intravenously at intervals of 8 hr. over as long as four weeks, are said to have no toxic effect whatever[7,8].

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L-Glutamine and the Growth of Embryonic Chick Tibiotarsi *in vitro*

In 1955 [1] Kieny published an account of the amino-acid requirements of eight-day embryonic chick tibiae cultivated on various simple mixtures of inorganic salts and amino-acids, including L-glutamic acid. She reported that although the addition of glutamine to the media caused some increase in the length of the bones they also lost weight. In a later paper[2], however, she concluded that the substance had no effect on the bones. Recently, Biggers, Gwatkin and Heyner[3] have described the growth of embryonic chick, rat and mouse tibiae on a relatively simple medium (denoted *BGJb*), which does not contain L-glutamic acid. It has been demonstrated in simple total deficiency experiments that L-glutamine is essential for growth in all three species, whether the response is measured in terms of length, wet weight or dry weight.

Other workers[4] have shown recently that explants of chick-heart tissue do not require L-glutamine because they contain glutamine synthetase. This enzyme catalyses the irreversible reaction:

L-glutamic acid + adenosine triphosphate + ammonia →
L-glutamine + adenosine diphosphate + phosphate

If we assume that glutamine synthetase is present in embryonic chick bones, then it is possible to argue that sufficient L-glutamine was synthesized from L-glutamic acid in Kieny's experiments to produce a maximal response. If so, then the addition of more L-glutamine to the system would produce no further effect. One can also argue that it is likely that some L-glutamine was formed to a minor extent in our experiments[3] since L-glutamic acid can arise from glucose in embryonic chick bones[5].

In order to settle these questions, the responses of seven-day embryonic chick tibiotarsi to different concentrations of L-glutamine have been studied in the presence and absence of L-glutamic acid. A 2×3 factorial arrangement has been employed: 1, 5 and 25 mgm. per 100 ml. of L-glutamine, and 0 and 25 mgm. per 100 ml. of L-glutamic acid, incorporated in all six treatment combinations in medium *BGJb*. In a preliminary experiment the concentration-response line of L-glutamine was determined. The results showed that the response becomes maximal in the range of 8·75–17·5 mgm. per 100 ml. Thus the concentration of 25 mgm. per 100 ml. which has been employed for the upper level of L-glutamine in the factorial experiment is more than sufficient to elicit a maximum response.

The uniformity of the paired limbs from embryos has been exploited by comparing the effects of the six treatments in a balanced incomplete block design. The pairs of tibiotarsi from fifteen embryos were allotted at random to the fifteen combinations between the six treatments taking two at a time. The bones were cultivated, using the floating lens paper technique, at 37° C. for 6 days in an atmosphere of humidified 5 per cent carbon dioxide in air. The medium was renewed every second day. At the end of the experiment the length of the bones was determined. The analysis of variance was done after converting all the data to logarithms. Only the intra-block error was estimated, and the adjusted treatment sum of squares were partitioned using the methods described by Kramer and Bradley[6].

The adjusted means are shown in Table 1, together with the analysis of variance. It is obvious that there is a highly significant linear regression of log length on the log concentration of L-glutamine in the medium and that some response occurred with only 1 mgm. per ml. L-glutamine in the medium. Since the L-glutamic acid and the interaction mean squares are not significant, there is no evidence that L-glutamic acid affects the response in length of the bones to L-glutamine. Thus there is no evidence that L-gluta-

Table 1. The Adjusted Mean Log Lengths (mm.) of Seven-day Embryonic Chick Tibiotarsi after Cultivation for 6 Days on Medium *BGJb*, in the Presence of Various Combinations of L-glutamine and L-glutamic Acid

L-glutamic acid (mgm. %)	L-Glutamine (mgm. %)		
	1	5	25
0	0·379	0·444	0·539
25	0·394	0·429	0·579

Mean initial log length 0·205.

Analysis of variance

Source of variation	D.F.	Mean square
Between embryos (unadj.)	14	0·0008
Between treatments (adj.)	(5)	
L-Glutamic acid	1	0·0008
L-Glutamine:		
Linear	1	0·0893*
Quadratic	1	0·0053
Interaction	2	0·0023
Intra-block error	10	0·0032

* $P < 0{\cdot}001$

mic acid is a precursor of L-glutamine in embryonic chick tibiotarsi, for if synthesis of L-glutamine did occur, the two concentration-response lines would be expected to separate, particularly at the lower levels of L-glutamine. Whether this is because this tissue does not contain glutamine synthetase remains to be determined.

The results also indicate why Kieny failed to demonstrate an effect of glutamine. The concentration used by her was only 0·16 mgm. per 100 ml., which is right at the lower end of the concentration-response line.

Hence, it is clear that L-glutamine is essential for the elongation of embryonic chick tibiotarsi *in vitro*, and that it is unlikely that it is produced from L-glutamic acid by this tissue. The importance of this compound to the cartilaginous rudiment is scarcely surprising in view of its essential role in the synthesis of purines[7] and chondroitin sulphate[8].

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Organization of Function in Trypanosome Flagella

Some cilia and flagella beat in a complex three-dimensional manner, and, in addition, the angular velocity at the tip is greater than at the base. Presumably the bundle of fibrils which make up a cilium or flagellum contains both conducting and contractile elements[1]. Trypanosome flagella, in common with most flagella and cilia, have 9 peripheral and 2 central fibres[2].

Acridine derivatives are well known to produce photosensitivity in cells and tissues. In the presence of pure 2 : 8-diamino-N-methylacridinium chloride (acriflavine) trypanosomes respond to light of wavelength 430–465 mμ first by an increased motility, secondly, by a stiffening of the flagellum which soon stops moving, and thirdly, by loss of refractility of the whole organism. To localize the site of photosensitivity a system of illumination was organized so that there was a circle of bright light about 4μ diameter and a background illumination of subdued red light to enable the operator to see a trypanosome throughout exposure without causing any additional damage.

The apparatus consisted of a microscope set up for Kohler illumination using a 6-V. 30-watt tungsten lamp. A ×40 objective (N.A. = 0·70) was used in place of the standard substage condenser and the trypanosomes were viewed through a ×80 oil immersion objective. An additional diaphragm held in a micromanipulator was placed close to the lamp house. This diaphragm consisted of an unprotected deep red gelatine filter (Wratten No. 70) which was carefully pierced with a pin from either side. The hole measured about 400μ in diameter. The image of this hole was formed in the plane of the object and was 4μ in diameter. A small circle of the same gelatine filter inserted into the eyepiece enabled the operator to observe both the trypanosome and the circle of light throughout an experiment.

Trypanosoma gambiense (an old laboratory strain) and *T. rhodesiense* (a newly isolated strain) were used in this experiment. The organisms were obtained from rat blood by centrifugation and diluted with a buffered-glucose Ringer's solution (*p*H 7·2) to give a count of about 12,000/μl. The final concentration of acriflavine was $10^{-5{\cdot}1}$ *M* for *T. gambiense* and $10^{-4{\cdot}91}$ *M* for *T. rhodesiense*; these concentrations were known from previous experiments to give complete immobilization in only a few seconds when the whole organism was illuminated. The movement of *T. rhodesiense* was reduced by the addition of 25 per cent of dextran powder (Benger, Ltd.) to the diluting medium. The temperature of incubation and exposure was about 20° C. No difference in behaviour was observed between the two species of trypanosome. The combined results are expressed in Table 1.

The circle of light was localized in one or more of the four regions *A*, *B*, *C* and *D* as indicated in Fig. 1.

When the circle of light was brought to bear on a trypanosome, increased motility was first observed. Continued exposure of any part of the flagellum produced a slowing of that part and movement usually ceased after 30–40 sec. (see Table 1). Exposure

Table 1. Details of the Response of Trypanosomes when Regions of the Cell are Exposed to Bright Light

Exp.	Region exposed	Time of exposure (min.)	No. of tryps. exposed	No. of tryps. responding	Response as regional motility *A*	*B*	*C*	*D*
1	*A*	<2	11	10	−	+	+	+
2	*A*	2–3	5	5	−	−	−	−
3	*B*	1	9	6	+	−	+	+
				2			+	+
4	(*C* + *D*)	1	13	12	+	+	±	−
5	(*C* + *D*)	>3	5	5	+	+	−	−
6	*D*	*c.* 1	3	3	−	−	+	−
	B	*c.* 1						
7	(*C* + *D*)	*c.* 1	4	3	−	+	±	−
	A	*c.* 1		1	−	−	−	−

Regional motility: − stationary; + passing waves; ± variable response or doubtful observation.

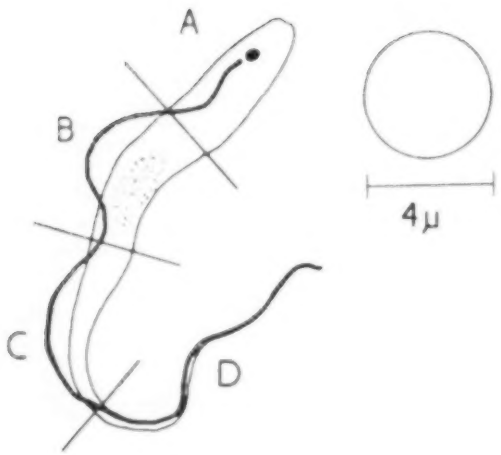

Fig. 1. Regions *A*, *B*, *C* and *D* of a trypanosome which were exposed to bright light. The circle, representing the area illuminated, is drawn to the same scale

for 1 min. of region *A* caused little obvious effect. Close examination after exposure revealed that the flagellum in this region neither accepted nor initiated any waves of contraction as it had done previously. Further exposure of region *A* caused sudden cessation of all movement of the flagellum and rapid loss of refractility of the organism. The time from full motility to this apparent state of death was less than 15 sec. in all cases. The total time taken for exposure of the region *A* to cause death was between 2 and 3 min. As the cone of light coming to a focus made an angle of 28° to the optic axis these longer exposures might have caused damage to other parts of the trypanosomes moving in and out of the cones of light above and below the focus. Exposure of the flagellum (*C* + *D*, group 5) for more than 3 min. showed that the action was specific to region *A*.

These findings can be summarized: In the presence of acriflavine, light on any part of the flagellum causes that part to stop moving, while the remainder of the flagellum continues to undulate. A similar quantity of light has no observable effect on the kinetoplast, but prolonged exposure of the kinetoplast results in death of the trypanosome.

As a rule, locomotion of trypanosomes occurs with the flagellum leading. A conducting element is therefore postulated to initiate waves of contraction that pass from the tip of the flagellum to the cell body. Groups 3 and 6 show that the flagellum behaves as though either a conducting element functions through the region of an injured contractile element or that contractions have local and self-initiated origins. In view of the cessation of all movement after prolonged exposure of the kinetoplast and of the complex screw-like waves which characterize flagellum movement in trypanosomes, it is suggested that contraction may be co-ordinated by information from the kinetoplast.

The observations qualitatively support the assumption made by Bradfield[1] that conducting and contractile elements are present in a flagellum. No evidence is provided on the mechanism of transmission of information along a flagellum, nor is it yet possible to localize, within the fibre bundle, these functional elements of conduction or contraction.

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RADIOBIOLOGY

Fatty Acid and Glucose Metabolism in the Perfused Heart

Previous work on intact animals in which arteriovenous differences across the myocardium were measured[1,2] have suggested that fatty acids are an important metabolite for the heart. No work has been reported on the isolated heart with radioisotopes which allow a separation of the uptake and fate of a particular substrate. This communication gives an account of the uptake and certain metabolic fates of fatty acid and glucose in the isolated, perfused heart. The results indicate the readiness with which the myocardium utilizes both glucose and fatty acids, and suggest that fatty acids are preferentially oxidized. The latter observation provides a possible explanation for the puzzling increase in cardiac glycogen known to occur with fasting or with untreated diabetes.

The isolated perfused rat heart described by Bleehen and Fisher[3] was used. This was modified as indicated by Morgan and Park[4] to permit the use of a low circulating volume. To measure formation of carbon dioxide labelled with carbon-14 from labelled substrates, a closed system was developed which included 15 ml. of Krebs–Henseleit bicarbonate solution and about 100 ml. of a gas mixture (95 per cent oxygen : 5 per cent carbon dioxide). Glucose (5 m*M*) and free fatty acid (0·4 m*M*) concentrations were within the physiological range for the rat. A 0·5 per cent solution of dialysed human serum albumin was used in experiments with free fatty acids. Male albino rats weighing 200–240 gm. were killed by decapitation after an overnight fast. No anticoagulant was used. Hearts were perfused with a substrate-free Krebs–Henseleit solution for 5 min., during which time the coronary flow, force, and rate of contraction became stable. Perfusion for 30 min. in the closed system followed. Then the hearts were weighed and digested in 30 per cent potassium hydroxide. Non-saponified lipids were removed by a single petroleum ether extraction. Following acidification to *p*H 1, tissue fatty acids were recovered by three petroleum ether extractions. Analyses for glucose, glycogen and for incorporation of carbon-14 into carbon dioxide, glycogen and fatty acids were essentially the same as described by Winegrad and Renold[5] for adipose tissue. Lactate was measured enzymatically[6] and free fatty acids by Gordon's method[7].

A summary of results is shown in Table 1. It will be seen that free fatty acids (0·4 m*M*), when present as the only substrate, are readily removed by the heart. When the fatty acids were labelled with palmitate-1-^{14}C nearly half the uptake was found in carbon dioxide. Palmitate label was also recovered to a significant extent in 'tissue fatty acids'; whether

Table 1. Uptake and Fate of Glucose-u-^{14}C (5 mM) and Palmitic Acid-1-^{14}C (0·4 mM) in Perfused Rat Heart

Substrate	No. of hearts	Uptake: Glucose	Uptake: FFA	Incorporation of label into: CO_2		Glycogen		TFA		Lactate	Residual glycogen	Label accounted for
		μM	μM	μM	Per cent	μM	Per cent	μM	Per cent	μM	μM	Per cent
FFA*	8	—	4·14 ±0·33	1·75 ±0·3	42 ±6	—	—	0·82 ±0·07	20 ±2	—	8·8 ±1·7	62
FFA* + glucose	6	19·9 ±4·7	3·96 ±0·4	2·12 ±0·4	54 ±2	0·006 —	0·07 —	1·00 ±0·09	25 ±2	—	11·8 ±0·7	79
Glucose* + FFA	10	23·7 ±1·8	4·88 ±0·2	0·52 ±0·08	2·2 ±0·1	0·73 ±0·23	3·1 ±1·0	0·005 (2)	0·005 (2)	36 ±6	11·9 ±0·8	54‡
Glucose*	12	20·8 ±1·2	—	5·1 ±0·8	17 ±2	0·44 ±0·05	1·45 ±0·2	0·01 —	0·02 —	43 ±8	9·6 ±0·9	62‡

All perfusions were for 30 min. Uptake, lactate production and label in CO_2, glycogen and tissue fatty acids (TFA) are expressed as μM/gm. wet weight/30 min.; residual glycogen as μM-glucose/gm. wet weight. Per cent = fraction of uptake.
FFA = free fatty acid (= unesterified = non-esterified fatty acid).
* ^{14}C labelled substrate.
† S.E. of mean.
‡ Sum of CO_2, glycogen and lactate (corrected for glycolysis during perfusion: in separate hearts the glycogen content after 5 min. perfusion with Krebs–Henseleit solution was 18·3 ± 1·2μM glucose/gm. wet weight) divided by uptake of glucose.

these represent fatty acids present in the tissue as free fatty acids or incorporation into triglyceride or other complex lipids has not been determined. Addition of unlabelled glucose (5 mM) to the perfusate had no effect on the uptake of free fatty acids; furthermore, the fraction of label from palmitate-1-^{14}C appearing in carbon dioxide and in tissue fatty acid was unchanged.

With glucose-u-^{14}C (5 mM) as the only substrate, 17 per cent of the uptake appeared as $^{14}CO_2$. There was definite incorporation of label into glycogen; essentially none was recovered as tissue fatty acid. Lactate production could account for 56 per cent of the glucose uptake and glycogen breakdown (Table 1). Addition of unlabelled free fatty acids (0·4 mM) strikingly reduced glucose oxidation to carbon dioxide. Under these conditions the uptake of glucose was slightly less, more residual glycogen was found after perfusion and more glucose carbon label was recovered in glycogen. No change in lactate production was observed.

The marked inhibition that free fatty acids exert on glucose oxidation to carbon dioxide suggests that fatty acids are preferentially oxidized when both substrates are present in the stated concentrations. It is unlikely that the reduced glucose oxidation to carbon dioxide produced by the addition of free fatty acids represents simply dilution of labelled carbon dioxide precursors by unlabelled substrate, since the addition of unlabelled glucose could not similarly alter the oxidation of palmitate-1-^{14}C. Furthermore, during free fatty acid inhibition of glucose oxidation, more of the glucose-u-^{14}C is incorporated into glycogen and the total myocardial glycogen is slightly increased. This suggests that the simultaneous presence of free fatty acids had diverted more glucose to glycogen synthesis with a net 'sparing' of cardiac glycogen.

Since fasting and untreated diabetes mellitus results in the mobilization of free fatty acids from adipose tissue these findings may explain the paradoxical observations that cardiac glycogen increases with fasting[7] and with untreated diabetes[8] in contrast to the depletion of glycogen in liver and diaphragm[9].

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HÆMATOLOGY

Site of Binding of Chromium-51 to Hæmoglobin

Gray and Sterling[1] have shown that when red blood cells are incubated with sodium chromate labelled with chromium-51, the latter enters the red cell and becomes firmly attached to intra-erythrocytic hæmoglobin. This tagging became the basis for *in vivo* studies of red cell volume and estimations of red cell life-span[2,3]. Despite its wide application in clinical medicine, little is known of the actual hæmoglobin-chromium-51 binding mechanism or site.

The molecule of normal adult hæmoglobin (*A*) has been shown to contain two pairs of distinguishable polypeptide chains (α and β) and can be schematically designated as $\alpha_2\beta_2$ (ref. 4). Most of the important abnormal hæmoglobins are altered only in the β chains. For example, hæmoglobin *C* can be represented as $\alpha_2\beta_2^C$ (ref. 5). Hæmoglobin *H*, an electrophoretically 'fast' variant, however, contains no α-chains and has been designated as β_4 (ref. 6). In acid solutions the hæmoglobin molecule undergoes asymmetric dissociation into free α_2- and β_2-units which

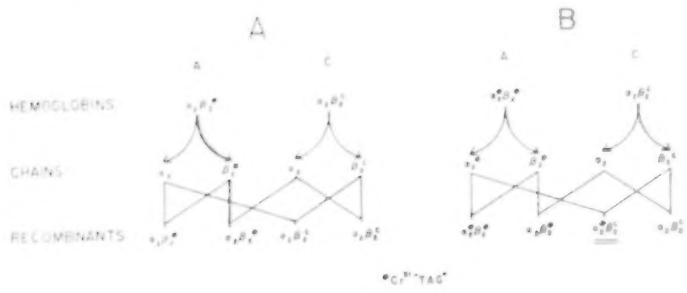

Fig. 1

recombine randomly when the solution is returned to neutral *p*H [7]. These facts have been utilized in this work in an attempt to elucidate possible sites of binding of chromium-51 to haemoglobin.

Red cells from a patient with haemoglobin *H* disease were tagged with iron-59 and chromium-51 as part of erythrokinetic studies. Haemoglobin solutions were made by haemolysis with toluene and cleared by ultracentrifugation. Oxyhaemoglobins *H* and *A* were separated by starch-block electrophoresis in phosphate buffer *p*H 7·0 in a 3-hr. run at 50 m.amp. and 400 V. The separated components were then analysed for haemoglobin content and for chromium-51 and iron-59 activity by γ-ray spectrometry in a sodium iodide well-type scintillation counter. Results are presented in Table 1.

Table 1

	Per cent of total haemoglobin	c.c./min. ^{59}Fe	Per cent of total ^{59}Fe counts	c.c./min. ^{51}Cr	Per cent of total ^{51}Cr counts
Haemoglobin *H*	18	16	20·5	1,107	33·7
Haemoglobin *A*	82	62	79·5	2,178	66·3

This indicates that the chromium-51 activity of haemoglobin *H* (β_4) is approximately twice that of equivalent amounts of haemoglobin *A* ($\alpha_2\beta_2$).

One explanation for the differences in chromium-51 activities of haemoglobin *H* and *A* would be that chromium-51 tags primarily to β-chains. To test this hypothesis, recombination experiments with chromium-51-labelled haemoglobin *A* and non-radioactive haemoglobin *C* were performed.

If chromium-51 binds only to β chains no radioactive haemoglobin *C* would be seen after recombination, since no 'hybrids' would be formed (Fig. 1*A*). On the other hand, if chromium-51 becomes attached non-specifically to both α- and β-chains, radioactive haemoglobin *C* would result, due to 'hybridization' (Fig. 1*B*).

Red cells from a normal person were labelled with chromium-51 and haemolysed immediately. Haemoglobin *C* was obtained from the haemolysate of a patient with homozygous haemoglobin *C* disease. Equal amounts of these solutions were mixed and then divided into control and reaction portions. Haemoglobin concentration of these was approximately 5·0 gm. per cent. The reaction portion was dialysed for 12 hr. against acetate buffer *p*H 4·7 and then returned to basic *p*H by successive dialysis against distilled water and barbital buffer *p*H 8·6. A precipitate was removed by high-speed centrifugation. Both control and reaction mixtures were converted to cyanmethaemoglobin and separated by starch-block electrophoresis in barbital buffer at *p*H 8·6 in a 16-hr. run at 48 m.amp. and 350 V. The fractions were then eluted and analysed for haemoglobin concentration and chromium-51 activity. Results are listed in Table 2.

Table 2

	Per cent haemoglobin		c.c./min. ^{51}Cr		Per cent ^{51}Cr activity	
	A	*C*	*A*	*C*	*A*	*C*
Control mixture	39·3	60·7	955	38	96·2	3·8
Reaction mixture	42·5	57·5	4,069	226	94·6	5·6

Similar results were obtained in experiments using haemoglobin *S* and agar electrophoresis. The reason for the chromium-51 activity in the haemoglobin *C* fraction is uncertain. Approximately 3 per cent can be accounted for by haemoglobin A_2 present in the *A* haemolysate and tagged along with haemoglobin *A* (unpublished observations).

Using two different experimental approaches, it has been shown that chromium-51 is attached to haemoglobin largely on the β-chains. Since the chromium-51 tag remains with the β-chain during dissociation and recombination, this may provide a useful tool for localizing altered polypeptide chains of abnormal haemoglobins.

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IMMUNOLOGY

Characteristics of γ-Globulin, lacking Antibody Properties, in New-born Pigs

In solving the problem whether γ-globulin lacking antibody properties exists and whether γ-globulin can be formed without an antigenic stimulus, our attention was focused on γ-globulin in piglets which had not been fed with colostrum[1]. The serum of piglets bred by a special technique without colostrum[2] is very suitable material for these experiments, because the placenta of these animals does not permit the penetration of γ-globulin[3], and the new-born animals lack this protein completely[4–8]. In our previous experiments[1], however, the presence of a detectable amount of γ-globulin has been demonstrated after 100 times concentration of the γ-globulin

fraction of the serum taken from the piglets bred under sterile conditions without colostrum for the first 14 days after birth; at that time piglets are not yet able to produce antibodies, not even against an artificially injected antigen (*Brucella suis*) nor against antigens naturally present (*E. coli* strains). This γ-globulin cannot combine with any of the tested antigens and it could therefore be described as 'normal' γ-globulin. By injecting methionine labelled with sulphur-35 to piglets bred without colostrum it was found that this small amount of γ-globulin was not transmitted passively from the mother by the intra-uterine route, but that the γ-globulin of the young animals was synthesized *de novo* during the period when the piglets were not yet producing antibodies.

In the present communication the results of physico-chemical and immunochemical investigations of γ-globulin of piglets which were bled shortly after birth without the intake of colostrum are presented. The γ-globulin was isolated from the serum by twice-repeated preparative electrophoresis on a starch block in veronal buffer, *p*H 8·6, Γ/2 = 0·05. The yield of the product which we called γ_N (γ-globulin neonatorum) was 50–80 gm. from 1 ml. of the serum. Paper and agar electrophoresis revealed a microheterogeneity typical of γ-globulins. The admixture of β-globulin was not detectable by paper and agar electrophoresis; its presence was demonstrated only using immunoelectrophoresis. Ultracentrifugation analysis indicates that the preparation γ_N contains a large component, apparently of a microheterogeneous nature, with a mean corrected sedimentation coefficient $S_{20,w} = 3{\cdot}1\ S$, and a small component with a sedimentation coefficient $S_{20,w} = 6{\cdot}1\ S$, contrary to the γ-globulin of adult pigs, which contains only components of 6·7 *S* and 18 *S*. The preparation was subjected to chromatography on *DEAE* cellulose in phosphate buffer, *p*H 8·0, with an ionic strength gradient according to Fahey[2]. The distribution of the proteins in the fractions is shown in Fig. 1. In order to carry out the immunochemical analysis of the separated fractions, two rabbit antisera were prepared. The first one was obtained by immunization of rabbits with electrophoretically prepared γ_2-globulin of adult pigs and was called anti-*PγGA*. The second one (anti-*PGN*) was obtained by immunization of rabbits with a fraction isolated by starch block electrophoresis from the γ-globulin area of new-born pig serum and containing γ- and β-globulins. Each chromatographic fraction was subjected to the agar precipitation test in Preer's modification. The precipitate with anti-*PγGA* serum appeared in fractions 13–30. This was a guide for making a sub-fraction γ_{N^-} which contained non-precipitating protein from the large frontal peak (about 50 per cent of protein γ_N) and γ_{N^-} containing protein precipitating with anti-*PγGA* (about 20 per cent protein γ_N). The sedimentation coefficient $S_{20,w}$ was 2·7 *S* for γ_{N^-} and 5·1 for γ_{N^+}. If γ_{N^-} is precipitated in immunoelectrophoresis with antiserum against piglet β- and γ-globulin (anti-*PGN*) at least four different components appear. Anti-*PγGA*, similarly as in Preer's modification, does not form any precipitate with γ_{N^-} in immunoelectrophoresis. That means that no antigenic determinant of γ_{N^-} is identical with γ-globulin of adult animals. γ_{N^+} precipitates in a single line with either of the antisera used. Anti-*PGN* precipitates also with adult γ_2-globulin, showing a double precipitation line. This is further evidence that serum of new-born pigs contains

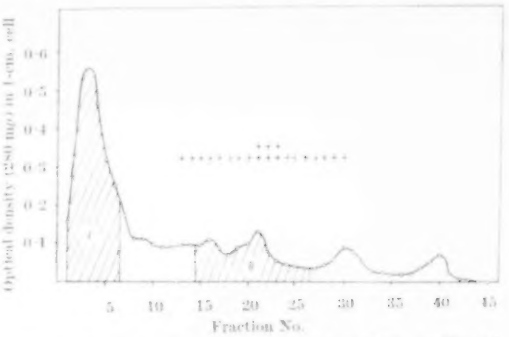

Fig. 1. Chromatography of γ_N on *DEAE* cellulose. Weight of protein, 25 mgm. Gradient from 0·02 *M* sodium phosphate, *p*H 8·0, to 0·3 *M* sodium phosphate, *p*H 8·0. Fractions in which precipitate with anti-*PγGA* serum was formed are expressed by crosses

proteins which possess at least some determinants of γ-globulin.

To elucidate completely the antigenic nature of γ_N and its relationship to γ_2 of adult animals a quantitative precipitation of anti-*PγGA* serum with antigens γ_{N^+} and γ_2 was carried out. The results of the precipitation in Fig. 2 show the sharp peak, contrary to the high and broad zone of maximal precipitation with γ_{N^+}. Although we cannot rule out that the preparation of γ_{N^+} contains protein which does not participate in the precipitation with anti-*PγGA* (for example, an admixture of β-globulin) the precipitation curves indicate quite clearly that γ_{N^+} is not fully identical with γ_2. If this were the case, both precipitation curves would fuse or have the same shape and be shifted on the antigen axis in the co-ordinate system used in Fig. 2. Since γ_{N^-}, which contains the components with the smallest sedimentation coefficients from the whole mixture, does not precipitate at all with anti-*PγGA*, it was investigated whether its possible antigenic relationship with γ-globulin will manifest itself by inhibition in the precipitation of anti-*PγGA* with γ_2 in the presence of excess of γ_{N^-}. In this test, γ_{N^-} behaved as a quite indifferent protein, and there is thus no evidence of its immuno-chemical relationship with γ-globulin.

Immunochemical data, together with the sedimentation and electrophoretic characteristic, thus indicate

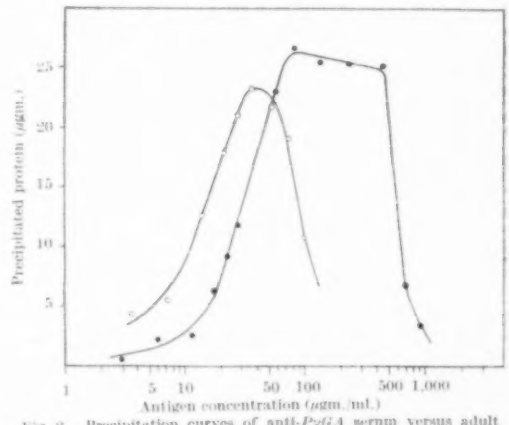

Fig. 2. Precipitation curves of anti-*PγGA* serum versus adult γ_2-globulin (open circles) and γ_{N^+} protein (solid circles)

that the serum protein of new-born pigs which is electrophoretically identical with γ-globulin contains components in close antigenic relation with γ-globulin of adult animals but immunochemically not identical. These components differ from γ-globulins of adult animals also by their molecular weight as shown by determination of a significantly lower sedimentation coefficient.

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Effect of some Metabolic Inhibitors on Antibody Formation

Recently the use of metabolic inhibitors, particularly analogues of nucleic acid components, has been proving an effective tool for investigating the processes involved in antibody formation[1–9]. The direct determination of the metabolic changes attendant on these processes is practically impossible at the present stage. After the first immunizing dose, only a very small proportion (about 1 per cent) of the lymphoid cells isolated from the spleen or the lymph nodes is active in antibody formation. The detection of any biochemical changes in these cells is made exceedingly difficult not only by the large 'background' of inactive cells (99 per cent) but also by the absence of serologically demonstrable antibody from the active cells in the initial (inductive) phase. Earlier I showed that the nucleic acid antimetabolite 6-mercaptopurine acts only during this inductive phase, but does not affect antibody production if administered during the productive phase[9]. If, then, antibody formation is inhibited by means of suitable agents without affecting protein synthesis in general, we may with some degree of plausibility draw conclusions about the processes taking place in the inductive phase.

The work to be described here, in which the effect of a variety of inhibitors was examined, was intended chiefly to show whether these inhibitors act directly by interference with intracellular metabolism, or rather indirectly through the inhibition of mitotic cell division resulting from their primary action. If it were possible to show that the inhibition of antibody formation is directly connected with the reduction of mitotic activity then this would constitute evidence for the validity of the clonal selection theory at the cellular level. A further objective of this work was, of course, the hope of finding compounds more effective in suppressing immunological response and less toxic than 6-mercaptopurine.

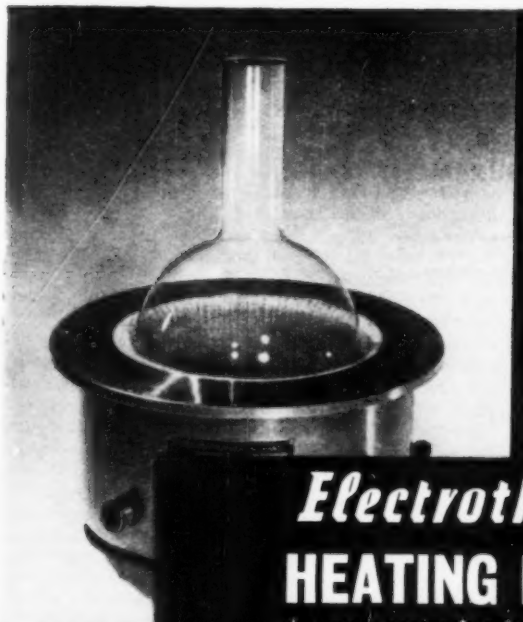
Inhibitory activity was determined by the same method as had been used in previous work with 6-mercaptopurine[9]. The cells isolated from the spleen of a normal non-immunized donor were mixed *in vitro* with *Brucella suis* antigen and injected intraperitoneally in a dose of 50×10^6 cells into three- to five-day-old rabbits. The antibodies produced by the transferred cells reach their highest titre 5–7 days after transfer, that is, at that stage in the development of the recipient when the latter is still incapable of responding to the antigen injected by antibody formation[10]. The evaluation of antibody response and its inhibition was confined to that stage (that is, the tenth to twelfth day of life of the recipients). The inhibitors were injected daily, for five days after transfer of the cells, at various dose-levels as indicated in Table 1 (only doses which were not yet fully toxic for the animal are recorded). In all, 400 neonatal rabbits were used in these experiments. The use of neonatal animals, which are more sensitive to the action of inhibitors[11], made it possible to distinguish more precisely between the general cytostatic effect of the inhibitors and their selective action on antibody formation.

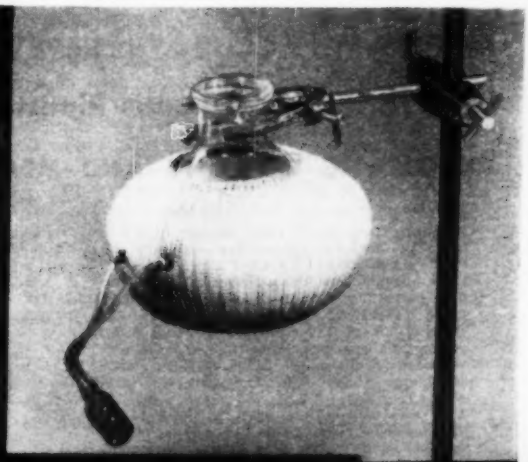
Table 1. Action of Metabolic Inhibitors on Antibody Formation

Type of inhibitors	Compound	Dose (mgm./100 gm. body-weight)	Inhibition of antibody formation
Pyrimidine antagonists	5-Fluorouracil	2·0*	0
		1·0	0
		0·5	0
	5-Bromouracil	5·0	0
	6-Azauracil	2·0	0
		1·0	0
		0·5	0
	6-Azauridine	500·0*	±
		50·0	±
		5·0	0
	6-Azauridine-monophosphate	4·0	0
	2-Thiouracil	5·0	0
		10·0	0
	4-Methyl-2-thiouracil	1·0	0
		5·0	0
	6-Azathymine	0·5	
	2-Thio-6-azathymine	2·0	0
	2-Thiothymine	2·0	0
Purine antagonists	6-Mercaptopurine	0·5*	+
		0·3	+
	8-Azaguanine	1·0	+
		0·5	0
	6-Thioguanine	0·1*	+
		0·05	+
Folic acid antagonist	Aminopterine	0·3	+
		0·15	+
		0·05	±
Inhibitors of mitotic division	Colchicine	0·3*	0
		0·2	0
	Demecolcine	0·1	0
	Actinomycin C	0·003*	0
Amino-acid antagonist	DL-Ethionine	5·0	0
Polyfunctional alkylating agents	*TS*-160 (trichlorethylamine)	0·1	0
	Myleran	2·0*	+
		0·5	0
	Leukeran	0·5	0

0, No significant inhibition of antibody formation; ±, inhibition significant in some animals; +, total inhibition in all cases.
*, Dose causing distinct toxic effects for the recipients of the spleen cells—new-born rabbits.

The inhibitors used included some analogues of the purine and pyrimidine bases, of folic acid, and of methionine, as well as some known cytostatics and polyfunctional alkylating agents. Table 1 summarizes the effects of some of these compounds. Inhibitory activity is found predominantly among the purine derivatives, whereas the pyrimidine derivatives do not inhibit antibody production. 5-Fluorouracil had no effect on antibody production at doses





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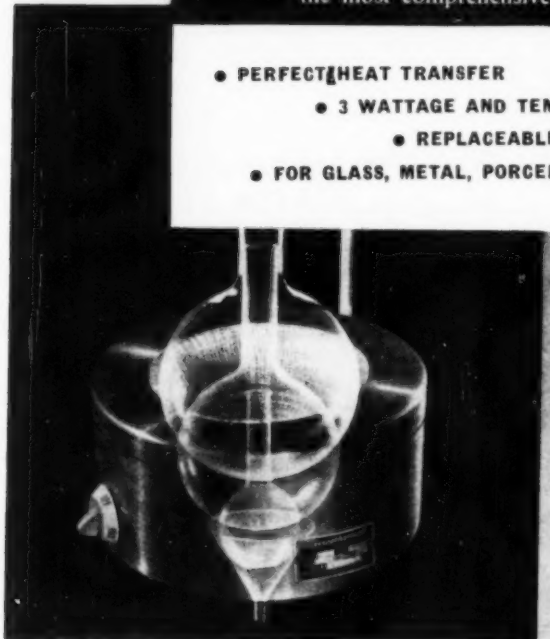

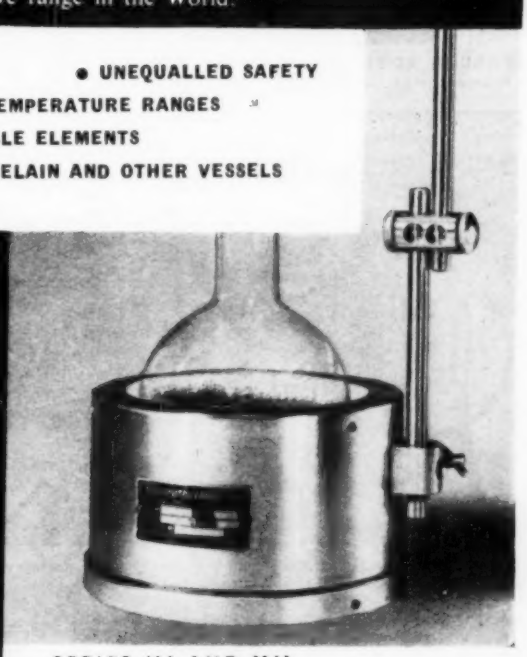

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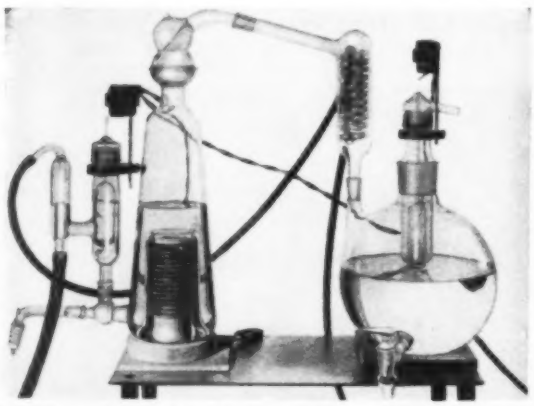

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which are known to be carcinostatic[12] and which were toxic for the neonatal rabbits. The only active pyrimidine antagonist was 6-azauridine (kindly supplied by Dr. J. Škoda, of the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Science; cf. ref. 13), but only in large, toxic doses (500 mgm./100 gm. body-weight). Since, of the purine analogues, the sulphur-substituted compounds were the most active, I also investigated a number of thio-compounds based on the pyrimidine skeleton (the compounds were kindly supplied by Dr. J. Gut, of the same Institute; cf. ref. 14); but the introduction of sulphur into the molecules did not lead to any enhancement of the activity.

The action of compounds known to inhibit cell division gave further information relevant to the question whether the formation of a cell clone is a pre-requisite for the induction of an antibody reaction. Injection of colchicine and actinomycin *C* in the highest possible doses was found not to affect the antibody response. These results accord with those obtained with 5-fluorouracil, which was also inactive in inhibiting antibody formation in doses which were generally cytotoxic.

Since other experiments have also indicated that the essence of the inductive phase does not lie in the multiplication of a predetermined type of cells under exposure to the antigen[15], it may be concluded that the effect of the active purine analogues on antibody formation involves direct interference with the adaptive metabolic processes which take place during the inductive phase.

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PATHOLOGY

Tissue Responses to Filter Membranes of Various Porosities

In the course of work on experimental silicosis in which diffusion chambers were used, it was discovered that the reaction of the tissues to the chamber varied greatly with the pore-size of the membrane of which its walls were made. The chambers were of the type used in earlier experiments[1] and the membrane was 'Millipore' type. The porosities tested were 0·65μ, 0·8μ, 1·2μ, 3μ and 5μ.

When placed within the rat's peritoneal cavity, each chamber is covered with mast cells and polymorphs within an hour. The mast cells rapidly disrupt and the granules enter the pores of the membrane; wherever the pores are full of 'cement', however, these cells remain intact. Within the next few hours large numbers of polymorphs enter the pores of the membrane, but comparatively few succeed in reaching the lumen of the chamber; most of them undergo rapid dissolution in the pores. Simultaneously, an inflammatory reaction develops in the adherent tissue which gradually increases until it is most intense after about three days. Thereafter, a fibrous reaction gradually develops so that, after 14 days, a dense fibrous capsule encloses the chamber. Half-chambers excite the same response as whole chambers (Figs. 1 and 2). The inflammatory reaction is most acute with membranes of 1·2μ, 3μ or 5μ porosity. With 0·8μ-pore membrane, however, the reaction is less acute: fewer polymorphs enter the pores and die there; no intact polymorphs reach the lumen of the chamber; the inflammatory reaction in the adherent tissue is less, and the fibrous capsule that forms is thinner. With 0·65μ-pore membrane, the majority of chambers do not even adhere to the omentum or mesentery: only a small number of polymorphs manage to enter the pores and, consequently, only a small amount of nuclear debris collects in the pores; the fibrous capsule is quite delicate.

Soaking the filter membrane in various solvents fails to make it less inflammatory. The only way to make it non-irritant to the tissues is to block the pores, either with 'cement' or by softening the membrane with acetone. In any event, the membrane is not toxic to cultures of *Strept. pyogenes*. There is no evidence therefore for the presence of a toxic contaminant.

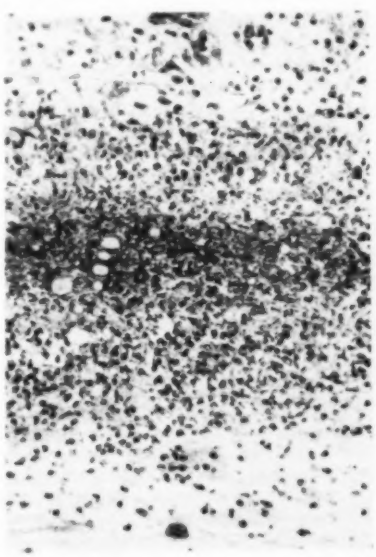

Fig. 1. Half-chamber made with 1·2μ-pore membrane after 2 days intraperitoneally. The membrane runs across the centre but is buried in inflammatory exudate. It is represented by the dark-staining band, which consists of the debris of polymorph nuclei within its pores. Inflammatory exudate covers both surfaces. (Hæmatoxylin and eosin. × 100)

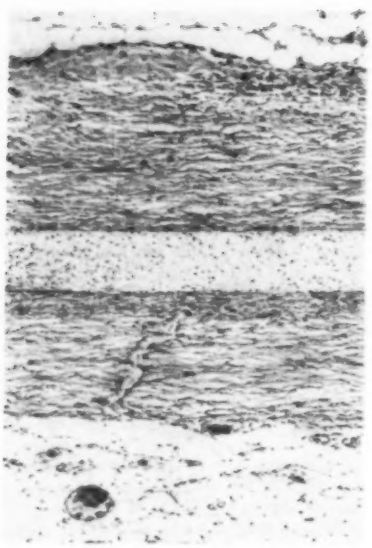

Fig. 2. Half-chamber made with 1·2μ-pore membrane after 14 days intraperitoneally. The membrane (centre) is now enclosed by a dense mass of fibrous tissue. Its pores contain only a few polymorphs. (Haematoxylin and eosin. × 65)

This acute inflammatory and fibrotic reaction was unexpected, because earlier experiments[1,2] showed that chambers made with 0·1μ-pore (or even 0·45μ-pore) 'Millipore' membrane did not adhere to tissues or excite an inflammatory reaction; and all 'Millipore' filters have the same chemical composition and the same weight of cellulose ester for a given size of filter, the only variable being the pore size. Since it seems that the intensity of the inflammatory reaction correlates with the ease with which polymorphs can enter the pores and die therein, the membranes may produce their effect by acting as a polymorph 'trap'. Clearly, if the dying polymorphs released an 'inflammatory' agent in the form of a vascular permeability-increasing factor, an inflammatory reaction would build up rapidly. This would be terminated only when fibrous tissue had sealed off the pores. On the other hand, there is the possibility that the migration and death of the polymorphs is secondary and merely one aspect of an acute inflammatory response initiated in some other way by the membrane. Permeability factors are becoming embarrassingly numerous and can be readily activated; for example, contact of serum with diethylaminoethyl cellulose during chromatography is sufficient to release one[3]. But, if the membranes are showing surface activity and releasing a permeability factor from the tissue fluids, it is difficult to explain why only the coarser-pore membranes do so, since, presumably, they expose a much smaller surface area to the tissue fluids than do membranes with finer pores (less than 0·45μ). Whatever the mechanism, it is interesting to find a chemically pure and 'inert' material capable of causing an acute inflammatory response and subsequent fibrosis because of a slight alteration in its physical form.

The significance of the mast cell response is difficult to assess. It was not caused by trauma, because these cells were intact over the 'cement-filled' areas. Since they do not react to smaller-pore (0·45μ or less) membranes, it is tempting to link them with the initiation of the inflammatory reaction; and, of course, they are well equipped to do so, since they contain histamine as well as serotonin and heparin. However, there is little other evidence to link mast cells with acute inflammation.

If disintegrating leucocytes could release a permeability factor, it would have a bearing on the problem primarily under consideration in these experiments, namely, how silica induces fibrosis. Little is known about the chemical mediators in chronic inflammation and fibrous repair, but it seems reasonable to assume that both processes are essentially manifestations of the sustained release in the tissues of a permeability factor. Such a factor would maintain a steady flow of fibroblasts and leucocytes from patent capillaries until sufficient fibrous tissue has formed to wall off the irritant. On this basis silica dust might be unique, not in its influence on fibroblasts, as is often assumed, but only in its ability to persist in the tissues and disintegrate the leucocytes which ingest it.

A more detailed account of this work will be published[4].

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BIOLOGY

Proposed Revisions of 'Transplantese'

The jargon employed by students of tissue transplantation has been named 'transplantese' by one of us[1].

Within a given species we wish to distinguish grafts exchanged between genetically identical individuals from those between genetically diverse individuals. Snell[2] suggested the word 'isograft' for the former and 'homoio-transplant' for the latter. Many people have remarked on the confusion arising from the use of isograft, which connotes genetic or antigenic uniformity, and 'isoantigen', which connotes the reverse. The latter is by far the older term and widely used by immunologists. As has been pointed out previously, transplantation immunity is but one facet of immunology, and a minority should try to conform to the terminology employed by the majority. There is also a more serious consideration which has been overlooked. The word 'isos' means 'equal', and 'homos' and 'homoios' mean 'the same'. It is therefore not logical to make the prefix 'iso-' denote a greater degree of similarity than 'homo-' or 'homoio-'.

Grafts between species are of less general interest. They have been called xenografts or heterografts.

Three adjectives related to the above nouns are in common use: 'isologous' (=genetically identical), 'homologous' (=of the same species, but not genetically identical) and heterologous (=of different species). Recently 'autologous' has disfigured the literature. This is not the place to discuss the origins and meaning of the termination '-logous', but it is not suitable for defining genetic relationships. 'Homologous' should always be used to denote some type of agreement or correspondence. There is no

possible justification for using the word to mean 'genetically different' since it is a flagrant contradiction of its proper use. 'Isologous' has no popular meaning; but, for the reasons stated above, it should not be made to denote a closer similarity than 'homologous'. 'Heterologous' is the correct antithesis of 'homologous', but it has no necessary reference to inter-specific differences. Indeed immunologists often use 'homologous' and 'heterologous' without any genetic connotation. The 'homologous' antigen is generally that used for immunization, and another antigen, even if derived from the same individual as the former, could be described as heterologous. The terms are often so used in discussions concerned with synthetic antigens. 'Autologous' is both meaningless and unnecessary.

One of us[1] suggested 'isogenic', 'allogenic' and 'heterospecific' in place of 'isologous', 'homologous' and 'heterologous', and we should like to reconsider these terms here.

So far as we can discover 'isogenic' was originally used to denote a population that was homozygous for all genes. The meaning seems to have been tacitly extended to cover other types of genetically uniform populations such as monozygotic twins and the F_1 between inbred strains. This being so there can be no possible objection to the use proposed above. However, we feel there is a need for a synonym that avoids the prefix 'iso-'. This is particularly needed with tumours. It is notorious that in the past so-called tumour-specific antigens have turned out to be isoantigens. There are now several examples of intra-strain immunity to tumours and it is most unfortunate that authors such as Hirsch[3] have used 'isoimmunity' in this context. We suggest the introduction of 'syngeneic' as a synonym for 'isogenic'. If one does not wish to refer to 'intra-strain immunity' one could then use 'syngeneic immunity'.

No objections have been raised against 'allogenic' as written, but in conversation it can be confused with 'allergenic'. We therefore propose 'allogeneic'; this should be pronounced 'allogeneeic', but even if pronounced 'allojeenic' it should not sound like 'allergenic'.

'Hetero-specific' has been used before and cannot be said to be illogical; but it is a Greco-Latin hybrid and we feel that 'xenogeneic' goes well with the other two terms we have suggested and is perhaps preferable.

We see no reason for any modification of 'autograft'. The adjective 'autoplastic' has been in use many years, and it does not seem justifiable to abandon it. A tumour growing in its original host has long been spoken of as 'autochthonous'.

'Homograft' and its commonly used synonyms are too firmly established and too useful to abandon. It must be realized that the term should embrace all types of intra-specific grafts and cannot be reserved for grafts between genetically diverse individuals. We cannot say that 'isograft' has proved a very fortunate term. Snell[2] originally intended it as an abbreviation of 'isogenic graft' although very few people seem aware of the fact. The expanded form is certainly preferable to that generally used. 'Isogenic homograft' is more precise. For reasons given above we feel there is much to be said for the employment of 'syngeneic homograft or graft'. 'Allogeneic graft' could, and probably will, be abbreviated to 'allograft'; but recent experience does not encourage premature abbreviation.

Table 1. PROPOSED REVISIONS OF 'TRANSPLANTESE'

Nouns			Adjectives		
Old terms	Proposed new terms	Alternative new terms	Old terms	Proposed new terms	Alternative new terms
Autograft	Autograft	—	Autologous	Autoplastic autochthonous (acc. to context)	
Isograft	Syngeneic homograft or graft	Isogenic homograft or graft	Isologous	Syngeneic	Isogenic
Homograft (general sense)	Homograft	—	Homologous	Allogeneic	—
Homograft (connoting genetic diversity)	Allogeneic homograft or graft	—			
Heterograft	Xenograft	Heterospecific graft Interspecific graft Heterograft	Heterologous	Xenogeneic	Heterospecific Heterologous

'Heterograft' is a relatively inoffensive term; but the meanings of 'heteros' and 'allos' are similar and do not provide a suitable contrast. We feel that the old term 'xenograft' is more explicit. The proposed alterations are shown in Table 1.

We should like to see international agreement on the terms to be used in this interesting field of study; but we cannot see any justification for continuing to antithesize sameness and equality in the perverse way that has commonly been done.

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Electrophoretic Patterns of Lymph Node Proteins in Hybrid F_1 Mice irradiated and treated with Myeloid and Lymphoid Cells from a Parental Strain

IT is generally admitted that graft antibodies do not circulate in the plasma and that graft immunity is carried on by cells from the lymphoid tissue and more precisely by those 'immunologically competent cells' of which the most striking features are their plasma cell-like morphological aspect and their high content of ribonucleic acid[1].

The purpose of this work was to find out whether graft immunization in lymph nodes will result in a modification of the electrophoretic pattern of the lymph node proteins as investigated by means of starch-gel electrophoresis[2]. It is implied that eventual modifications in patterns could correspond to the graft antibody located inside the immunized cells.

(*a*) In a first group of experiments, we have studied the lymph nodes of the host in connexion with a graft of lung tissue. The nodes were removed 5–7 days after insertion of the graft. Genetically the systems used herein were as follows: Host: *C57Bl6*; donors: *DBA2*. Hosts: *DBA2*; donors *C57Bl6*. Hosts: *C57Bl6*; donors (*C57Bl6*. *DBA2*)F_1.

In all these cases the lymph node content in hyperbasophilic cells was moderately increased, up to 4 and 6 per cent. The electrophoretic patterns of the lymph node proteins were apparently similar to those of lymph nodes from non-grafted mice, *C57Bl6* or *DBA2* or F_1 taken as controls and also to those of mice grafted with isogenic lung grafts. In the latter the number of cells with hyperbasophilic cytoplasma was normal.

(*b*) In a second group of experiments, we have studied the lymph node proteins of (*C57Bl6*.*DBA2*)F_1 receiving a whole-body irradiation of 500 rads (200 kV., 50 cm. distance, 12 m.amp., 0·5 aluminium, 0·5 copper) and injected 24 hr. later with 2×10^7 bone marrow cells and 2×10^7 lymph node cells from the parental strain *C57Bl6*.

In this group, we actually observed in the lymph nodes a definite reaction of immunologically competent grafted cells against the antigens of the host. The number of hyperbasophilic cytoplasm cells seven days after grafting was considerable, reaching a percentage of more than 40 (ref. 3). When extracts of these lymph nodes were submitted to electrophoresis through starch gel, an extra band (Fig. 1) appeared which does not exist in extracts of lymph nodes from untreated mice nor from mice injected with bone marrow and lymph nodes cells from isogenic donors: F_1 injected with F_1 cells, *C57Bl6* injected with *C57Bl6* cells.

Within the limits of our experiments, it can be asserted that this particular band shows only when: (*a*) there is a transplantation immunological reaction which in this particular case was a reaction of the grafted cells against the antigens of the host that the grafted cells did not possess; (*b*) when the number of hyperbasophilic cytoplasm cells is very high.

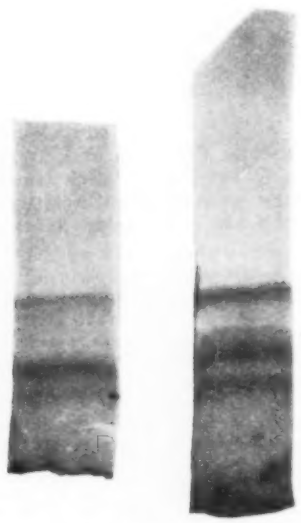

Fig. 1

Only the cathodic fraction of the gel is represented on the figure

It is not unreasonable to assume that the band shown in starch gel whenever an immunity reaction takes place in the lymph nodes together with the striking increase in number of hyperbasophilic cytoplasma cells might correspond indeed to the production of the antibody.

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Lysine Synthesis and Phylogeny of Lower Fungi: Some Chytrids versus *Hyphochytrium*

Recent work, conducted with the aid of various diagnostic carbon-14 tracers, has suggested that lysine biosynthesis is a valuable character in the detection of certain evolutionary relationships[1–4]. All the eubacteria, pseudomonads, actinomycetes[1], green algae[2], and higher (vascular) plants[3] examined appear to synthesize lysine in one general manner (presumably via α,ε-diaminopimelic acid, cf. ref. 5) and all the ascomycetous and basidiomycetous fungi[1,2] (and also *Euglena*[2]) in another (presumably via α-aminoadipic acid, cf. ref. 6). Among the lower fungi (phycomycetes), a striking dichotomous distribution of the two lysine paths was noted: the Mucorales and Blastocladiales studied, like the higher fungi, evidently use the path via α-aminoadipic acid, and the Saprolegniales that via α,ε-diaminopimelic acid[4]. The present communication reports findings with some other phycomycetes, including three chytrids and a representative of the Hyphochytriales. The latter group of organisms, although closely paralleling the chytrids in body structure, have uncertain phylogenetic affinities.

The formation of lysine in the phycomycetes selected was investigated with the aid of radioactive DL-aspartate, DL-alanine, and acetate. Table 1

Table 1. Incorporation of Tracers into Protein Amino-acids of *Rhizophlyctis rosea* and *Hyphochytrium catenoides* (as Specific Activity Relative to the Respective Protein Aspartic Acid Values)

Organism	Tracer	Aspartic acid	Threonine	Lysine
R. rosea	[4-^{14}C] Aspartate	100	104	< 5
R. rosea	[1-^{14}C] Alanine	100	95	< 5
R. rosea	[2-^{14}C] Acetate	100	91	440
H. catenoides	[4-^{14}C] Aspartate	100	94	107
H. catenoides	[1-^{14}C] Alanine	100	91	134
H. catenoides	[2-^{14}C] Acetate	100	90	90

The organisms were cultivated in 20 ml. of glucose-salts medium in 250-ml. flasks at 28° C., *R. rosea*, without shaking, in the medium of Stanier (ref. 7) and *H. catenoides*, with shaking, in that of Fuller (personal communication). Approximately 2–5 mgm. (20–50 μc.) of tracer were supplied per flask. For the determination of relative molar amounts of the three protein amino-acids, experiments with uniformly labelled glucose were performed. The cultures obtained were subjected to the collecting, extraction, hydrolysis, paper chromatography, and counting procedures previously described, and specific radioactivities of the protein amino-acids were computed on a molar basis, as before (refs. 3 and 8).

shows the labelling pattern found for the chytrid, *Rhizophlyctis rosea*, strain *QM*, obtained through the courtesy of Dr. J. N. Couch, and for a strain of *Hyphochytrium catenoides*, isolated by Dr. Couch and kindly furnished by Dr. M. S. Fuller. In the case of the former organism, the 4-carbon of aspartate and the 1-carbon of alanine are not appreciably incorporated into protein lysine, whereas the 2-carbon of acetate labels lysine heavily (in comparison with the labelling of protein aspartic acid and threonine). Essentially the same behaviour was shown by two other chytrids (generously provided by Dr. Couch and Dr. Fuller, respectively): *Phlyctochytrium punctatum*, strain *NG-3* (ref. 9) and an organism similar to strain *QM*. In the case of *H. catenoides*, the 4-carbon of aspartate and the 2-carbon of acetate make approximately equal relative contributions to protein lysine, aspartic acid, and threonine; the 1-carbon of alanine contributes somewhat more extensively to lysine than can be accounted for by the conversion of the alanine to aspartic acid. In experiments with DL-[3-^{14}C] aspartate, the chytrids as well as *H. catenoides* showed substantial incorporation of carbon-14 into lysine. With regard to these labelling patterns, which will be discussed in more detail elsewhere, the chytrids are like the Blastocladiales, Mucorales, and higher fungi (as well as *Euglena*) and presumably have the α-aminoadipic acid–lysine path, whereas *H. catenoides* resembles the Saprolegniales and green algæ (as well as bacteria and vascular plants) and appears to use the α,ε-diaminopimelic acid–lysine path. It is noteworthy that the path via α-aminoadipic acid has thus far been indicated exclusively in those phycomycetes producing posteriorly uniflagellate zoospores or aplanospores, and the path via α,ε-diaminopimelic acid in those producing biflagellate or anteriorly uniflagellate zoospores.

The present results strengthen the view that the mode of lysine synthesis is a useful character in the exploration of certain phylogenetic links. The utility of this character is thought to depend in part on the fact that each of the two pathways contains a number of enzymes that appear to be specifically concerned with the formation of lysine. The two sets of enzymes are thus presumed to represent a considerable period of evolution and are viewed as biochemical organelles of ancient origin.

Grateful acknowledgement is made of the generous helpfulness of Dr. J. N. Couch and Dr. M. S. Fuller. Excellent technical assistance was provided by Mrs. Helen Carnevale. This work was aided by the National Science Foundation and by the Office of Naval Research.

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Growth of Embryonic Mammalian Cartilage after Freezing

SINCE the discovery that glycerol will protect cells and tissues against freezing damage[1], considerable progress has been made in developing techniques for the preservation of tissues at very low temperatures. Attempts to establish low-temperature banks of adult human cartilage have unfortunately, so far, proved unsuccessful[2]. Biggers[3], however, was able to show that embryonic chick tibiæ will grow and differentiate *in vitro*, after freezing to −79° C., in saline containing 15 per cent glycerol. This communication describes briefly some of the work concerned with freezing embryonic rat tibiæ to −79° C. A fuller account is being given elsewhere[4]. Rat fœtuses of a known age were obtained from the Medical Research Council strain of albino rat, bred in the Department. The occurrence of a vaginal copulation plug, or the presence of sperm in the vaginal smear, was taken as the indication of mating. On the seventeenth day *post coitum*, the conceptuses were excised, and the embryonic tibiæ were isolated under a dissecting microscope. The bones were cleaned of as much extraneous tissue as possible, with care to avoid injuring the perichondrium. The structure of these tibiæ is being described elsewhere[5].

The embryonic bones were cultivated *in vitro* using either the plasma clot technique[6] or the floating-lens paper method[7]. The cooling technique employed was that described by Smith[8], and in all cases the frozen bones were thawed rapidly.

A preliminary series of experiments investigated the growth of 17-day embryonic rat bones after they had been equilibrated for various lengths of time in saline or plasma containing 15 per cent glycerol and then either frozen or explanted without freezing. Both the frozen and the unfrozen bones were rapidly rinsed in Tyrode's solution to remove any residual glycerol before they were explanted. In all these experiments, the frozen bones showed no subsequent elongation *in vitro*. Of the unfrozen bones, those which had been exposed to a concentration of 15 per cent glycerol, for periods not exceeding 30 min., elongated in a normal manner; those unfrozen bones that had been exposed to higher concentrations of glycerol-plasma, or for extended equilibration periods, did not afterwards elongate.

It was then decided to use trypsin, in an attempt to discover whether chondrocytes which were partially freed from their matrix would survive freezing. Tibiæ and femora from 17-day-old embryonic rat tibiæ were chopped into two or three pieces and digested with trypsin, using the method of Moscona and Moscona[9]. Tryptic digestion was carried out until the matrix was viscous and jelly-like, but the cells were still embedded in the matrix. The trypsin-treated cartilage was then suspended in 15 per cent glycerol plasma, and equilibrated for 30 min. at room temperature. Two thirds of the fragments were then cooled slowly to −79° C. and kept at this temperature for 1 hr. The remaining unfrozen fragments were briefly rinsed in Tyrode's solution to remove any residual glycerol and explanted. The frozen fragments were thawed rapidly, rinsed in Tyrode's solution, and explanted. Each culture contained fragments from approximately two bones. The explants were cultivated for five days and were sub-cultured after three days *in vitro*. Cartilage which survived the experimental treatments appeared healthy and viable; the amorphous fragments

rounded up into whitish opaque nodules, regaining a definite shape after approximately 12 hr. *in vitro*. The nodules increased in size during the cultivation period, and, in addition, there was a peripheral outgrowth of clearly visible fibroblasts, growing in a radial pattern.

A similar experiment was carried out with cartilage from 18-day rat embryos. The tibiæ and femora were fragmented and treated in exactly the same way as described previously. As there appeared to be no difference between the survival of 17- and 18-day embryonic cartilage, or between tibiæ and femora, the results were combined and are shown in Table 1.

Table 1. Results obtained after slowly freezing Embryonic Rat Cartilage from 17-day and 18-day Tibiæ and Femora to −70° C. The Cartilage was pretreated with Trypsin and suspended in 15 per cent Glycerol-Plasma

	Killed	Survived	Total
Frozen	4	10	14
Unfrozen	1	9	10
Total	5	19	24

The probability of these results, or more extreme ones, arising from chance, was calculated using Fisher's exact method[10]. The probability was found to be $P = 0{\cdot}566$; thus, although there is a suggestion that the frozen cultures had a greater mortality than the non-frozen cultures, on the data obtained, this is nowhere near significant at the conventional $P = 0{\cdot}05$ level.

Histological examination of the explants which survived the experimental treatments revealed that both the rounded epiphyseal and the hypertrophic diaphyseal cells survived the freezing. The morphology of the cells was normal; and when the sections were stained with toluidine blue, the characteristic metachromasia of the matrix was seen.

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Temperature Coefficient of Endodiurnal Leaf Movements in *Phaseolus*

The effect of temperature on the length of cycle of endodiurnal rhythms has been investigated in various processes in plants and animals. It was repeatedly found that within the physiological range the length of cycle is independent of temperature[1–3]. Several other endodiurnal rhythms, however, showed various temperature coefficients between 0·8 and > 3 (refs. 4–6). Went[7,8] reported a temperature coefficient in leaf movements of *Phaseolus* of 1·2 which is in agreement with early observations of Bünning[9]. Went, however, does not state under what conditions his plants were grown before measuring the cycle. As I have pointed out[10], the external conditions under which the seedlings are grown will determine the response. Etiolated plants, grown at 15, 20 and 25° C., showed a constant cycle-length of 28·0–28·3 hr. When the plants were grown in the greenhouse and then transferred to constant conditions, a Q_{10} of 1·2 was observed for the first two cycles; the Q_{10} changed in the subsequent cycles to 0·9, thus revealing a temperature-compensating mechanism.

Went's statement[7] that my investigations "did not give any temperature effects on the cycle length but showed a constant 24-hr. cycle over a whole range of temperatures" is erroneous. I did not report a 24-hr. cycle in leaf movements. Went implies that a 24-hr. cycle of smoke and fog governed the leaf movements in my investigations. This assumption cannot be maintained since a cycle-length of 28 hr. was observed in etiolated plants. Furthermore, greenhouse-grown plants, measured at 20° C. at constant darkness, showed over five days a constant cycle-length of 26·1–26·7 hr. This finding by Lörcher[11], who used the same facilities as mine, does not reveal effects of external factors operating in regulating the *Phaseolus* clock.

Increased variability in the cycle-length under constant conditions[10] also indicates that the leaf movements were not controlled by external factors.

I showed that greenhouse-grown plants exhibit after transfer to constant conditions in the first two cycles after the transfer a Q_{10} of 1·2 the same coefficient as found by Bünning and Went. Whether or not the length of cycle is altered by temperature, however, is largely dependent on the pretreatment of the seedlings.

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The Northern Rockling in the Clyde Sea Area

On August 15, 1960, a northern rockling, *Ciliata septentrionalis* (Collett 1875), was caught in the Clyde Sea area. The fish was caught at a depth of 30–40 fathoms in a small mesh cover that had been fitted over the cod end of a trawl used by R.V. *Calanus*. It is 10·6 cm. in length and agrees closely with the descriptions of Smitt[1] and Schnackenback[2].

This is the first record of *Ciliata septentrionalis* from Britain. Elsewhere it has been recorded in Norway between 70° 13′ N. and Bergen[3] and from south Greenland[4]. I have previously found two specimens in a jar in the Sales Department here, but there was no record of when the fish were preserved, who preserved them or where they came from. However,

it now seems probable that the fish lives permanently in the Clyde.

T. B. Bagenal

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BACTERIOLOGY

Variation of Elasticity along Single Microfibrils of Bacterial Cellulose

A NUMBER of models have been proposed for the internal fine structure of individual cellulose microfibrils which suggest variability both across and along the axis of the microfibril. Frey-Wyssling[1] has suggested that microfibrils are subdivided into four continuous crystalline strands, each about 70 A. wide, which run parallel to the microfibril axis and are held together by a paracrystalline matrix. In contrast, Preston[2] has concluded that cellulose microfibrils from algae are composed of a paracrystalline sheath surrounding a highly crystalline single core which is interrupted at random positions by less-crystalline material labile to electron bombardment. The positions occupied by this material may coincide with the sites of trace residues (*Fremdgruppen*) postulated by H. K. Meyer and van der Wyk and by Treiber[3].

In this contribution is presented direct evidence for random variation of elasticity along the length of individual microfibrils of bacterial cellulose.

Cellulose-free, washed cells of *Acetobacter xylinum* were prepared as described previously[4], and 1 ml. of the suspension used to inoculate 35 ml. of sterile medium[5] in Petri dishes, 10-cm. in diameter. Sterile microscope slides were slipped beneath the surface of the medium, and on top of the slides were placed several sterile copper electron microscope grids. Each culture was incubated in covered Petri dishes 4–12 hr. at 30° C. The glass slides carrying the electron microscope grids were gently lifted from the medium (horizontally) and air dried. The dried slides were washed in a slow current of water with a minimum of agitation. The grids with adherent microfibrils were again dried, shadowed with palladium–gold (60 : 40) at an angle of 15° to increase electron scattering and examined.

Examination at low beam intensities showed single straight microfibrils or straight bundles of microfibrils extending over distances of more than 70μ without support. As beam intensity was increased, the single microfibrils or bundles began to coil into rough irregular helices (Fig. 1), presumably because of differential heating of the shadowed and unshadowed halves of the microfibrils. The degree of coiling depended on the maximum intensity to which the microfibrils were exposed and was irreversible.

No appreciable relaxation of the microfibrils to their original straight form was observed on reduction of beam intensity, but an extension or contraction of the coil on variation of beam intensity was often seen. That the coiled microfibrils were under severe longitudinal strain was shown by frequent snapping and sharp recoil of the threads to form tangled clumps

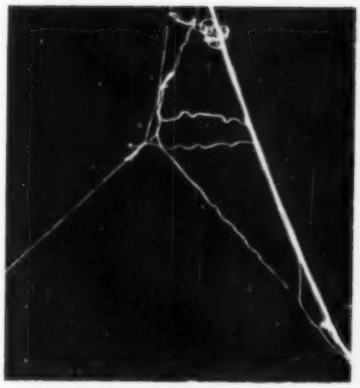

Fig. 1. Helices of bacterial cellulose microfibrils formed by heating shadowed straight microfibrils or bundles in an electron beam. Note tangled clump of microfibrils, formed after breaking in the electron beam

(Fig. 1). The twisting of individual microfibrils exhibited their flattish ribbon-like outline clearly (Fig. 2).

The most interesting property shown by the above helices was the marked variation in coiling of the same microfibril or bundle of microfibrils from point to point along its length (Fig. 3). Not all microfibrils were coiled, perhaps because of the extreme tension to which some were subjected, but of those which did the pitch of the helix often changed abruptly. Since the total stress was the same at any point of an unsupported segment of a single microfibril, this variation in pitch must reflect a corresponding variation of elasticity at different portions of the thread. Similarly, in a bundle of microfibrils, variation of the pitch of the helix of the bundle must reflect a variation of the composite bundle modulus, which in turn implies variations of the modulus in single microfibrils. Since the angle and degree of metal shadowing, as well as the electron-beam intensity, were uniform along any initially straight microfibril, the above variation in elasticity may be attributed to either a corresponding variation in twisting of the

Fig. 2. Single twisted bacterial cellulose microfibrils. Inset: Note end of broken microfibril which may be frayed

Fig. 3. Helical microfibrils showing the abrupt variation in pitch along their length

original microfibrils or to variations in the fine structure of straight ones. However, if the original microfibrils are irregularly twisted, this also implies a linear variation of internal fine structure. Thus either attribution points to a variation of fine structure along single microfibrils. This variation may be due to differences in crystallinity along the microfibril, differences in the number of β-glucosan chains composing the microfibril at various points, variations in the type of packing of glucose residues within the unit cell or variations in the local content of trace residues along the microfibril.

The random variation of tensile strength along microfibrils of bacterial cellulose suggests that their fine structure is closer to the model proposed by Preston for *Valonia* cellulose than that suggested by Frey-Wyssling, since variations along four crystalline continuous sub-filaments would tend to cancel out. Also, if sub-filaments existed in single microfibrils of bacterial cellulose, fraying on breakage should be evident; but only one tentative instance out of several hundred was noted (Fig. 2). This single observation may also be attributed to irregular fracture along a solid core and is therefore not conclusive.

Since bacterial cellulose microfibrils grow at the tips[4,6], the observed variation in tensile properties implies corresponding deviations in the detailed mechanism of deposition and crystallization of individual glucose residues during fibrogenesis. Such deviations, however, must be only digressions from a stable process since clearly they are corrected quickly. The inference of such temporary deviations is also supported by Rånby's recent observation that bacterial cellulose microfibrils which have never been dried have approximately 25 per cent more accessibility to tritium atoms than the same material after drying[7].

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GENETICS

Genetic Recombination in *Vibrio cholerae*

The occurrence of genetic recombination in *V. cholerae*, revealed by crosses between double auxotrophic mutants of strain 162, was mediated by a fertility factor—designated the *F* factor—which could be infectively transmitted from strain to strain by conjugation[1]. F^+ strains (possessing the fertility factor) gave rise to recombinants when crossed with F^- strains (devoid of the fertility factor).

The relative roles of F^+ and F^- strains in such crosses have now been elucidated. When F^+ strains, suspended in minimal medium, were exposed to ultra-violet light to reduce their viable count by a factor of 1/1,000 to 1/10,000 and then crossed with normal F^- strains there was a considerable stimulation of recombination as judged by the number of colonies which appeared on selective media. If, on the other hand, F^- strains were likewise exposed to ultra-violet light to effect a similar reduction in viable count and then crossed with normal F^+ culture, recombination was almost completely abolished. This differential effect of ultra-violet light has been confirmed in four different crosses between F^+ and F^- mutant stocks. Table 1 furnishes details of one such cross. F^- strains grown in broth culture supernatants of

Table 1. Effect of Ultra-Violet Irradiation of Parent Strains on Genetic Recombination in *Vibrio cholerae* Cross V44F^+ (*pur*, *arg*, *str-r*, 200-*r*) × V39F^- (*ilvα*, *str-s*, 200-*s*)

Cross	No. of viable cells of each parent in the cross	No. of colonies (in duplicate plates)			
		purine minimal agar		arginine minimal agar	
V44F^+ × V39F^-	$1{\cdot}7 \times 10^8$ + $2{\cdot}5 \times 10^8$ $6{\cdot}0 \times 10^7$ + $8{\cdot}0 \times 10^7$	193 74	191 57	25 10	25 11
V44F^+ (U.V.) × V39F^-	$1{\cdot}0 \times 10^8$ + $2{\cdot}5 \times 10^8$ $3{\cdot}0 \times 10^8$ + $8{\cdot}0 \times 10^7$	*c.* 1,000 150	*c.* 1,000 154	232 56	253 54
V44F^+ × V39F^- (U.V.)	$1{\cdot}7 \times 10^8$ + $2{\cdot}3 \times 10^8$ $6{\cdot}0 \times 10^7$ + $8{\cdot}0 \times 10^7$	nil nil	nil nil	nil nil	nil nil
V44F^+ (U.V.) × V39F^- (U.V.)	$1{\cdot}0 \times 10^8$ + $2{\cdot}3 \times 10^8$ $3{\cdot}0 \times 10^8$ + $8{\cdot}0 \times 10^7$	3 nil	4 nil	nil nil	nil nil

U.V., irradiated with ultra-violet light; 200-*s*, sensitivity to phage 200; 200-*r*, resistance to phage 200; *pur*, *arg*, requirement for purine and arginine; *ilvα*, requirement for valine and isoleucine; *str-s*, sensitivity to streptomycin; *str-r*, resistance to streptomycin.

irradiated P^+ cultures did not give rise to recombinants.

The differential lethal effect of ultra-violet light on P^+ and P^- strains shows that recombinants arise from the P^- parent, which probably functions as a gene-acceptor. P^+ strain appears to be a gene-donor, the viability of which is not essential for the expression of the recombinants.

A similar situation is now well recognized in *Escherichia coli*[2,3] in which it was first demonstrated by the differential effect of streptomycin[4] on F^+ and F^- strains. The streptomycin method was not suitable for *V. cholerae*, as it resulted in a marked reduction in recombination-rate. Nevertheless, a significant number of recombinants could be obtained when P^+ strains were treated with streptomycin and crossed with P^- cultures and none at all if P^- strains were treated with streptomycin and crossed with P^+ cultures. Full details of this work will be published elsewhere.

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Histocompatible Colour Mutant from *CBA/Lab* Strain of Mice

The progeny from a breeding pair of *CBA/Lab* mice, a strain which is propagated by brother × sister mating, were found to have grey agouti coats in contrast to the usual wild-type agouti of the strain. These '*CBA* grey' mice when mated together produced similar 'grey' mice among their progeny (that is, the 'grey' character behaved as if it were determined by a recessive gene), and it was thought to be of interest to test the original strain and its mutant for histocompatibility.

The results are shown in the photographs of skin grafts from normal *CBA* and mutant animals on a *CBA* mouse (Fig. 1) and on a mutant *CBA* mouse (Fig. 2) indicate histocompatibility between the two

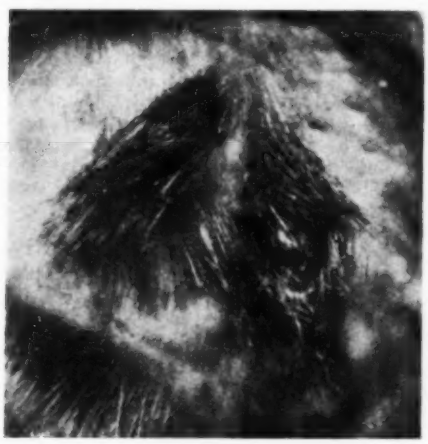

Fig. 1

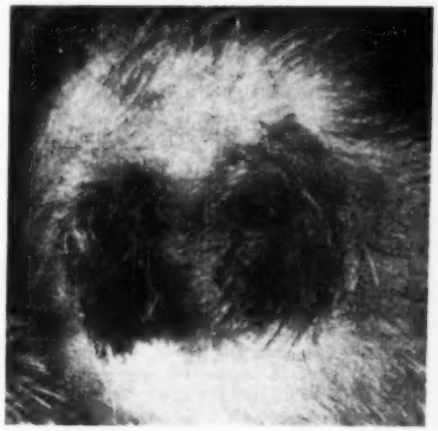

Fig. 2

lines. A similar compatibility to skin grafting between a *CBA* mutant *p* (pink eye) and its host was found by Fraser and Clayton[1]. In a later communication given in the Institute of Animal Genetics Research Report 1955–1957, Mrs. Clayton refers to antigenic differences between these two types.

Preliminary tests by Dr. Mary Lyon of the Radiobiological Research Unit, Harwell, to determine the gene that our mutant carries have shown that grey is not the same as or allelic with genes *a*, *b*, *ech*, *d*, *pa* or *p* (pink eye). This does not necessarily mean that it is a new mutant, and further tests are progressing

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PSYCHOLOGY

Theory of the Visual Threshold

Gregory[1] and Cane and Gregory[2] have put forward a theoretical equation for the brightness increment threshold considered as a statistical discrimination. For a given frequency of detection they propose that:

$$\frac{[(r + \Delta r) - r] - C}{\sqrt{\left(\frac{1}{A_1} + \frac{1}{A_2}\right) V}} = \text{const.} \qquad (1)$$

where $(r + \Delta r)$, r, are the mean neural pulse-rates associated with the intensities $(I + \Delta I)$, I, and V is the variance of these rates. C is a constant necessary to account for the occurrence of fewer than 50 per cent false positives. Its implication, as stated by Gregory, is that "some fixed difference between impulse rates is required before discrimination is established, this difference being independent of the intensity I".

This equation can be regarded as an adaptation of Thurstone's[3] law of comparative judgment, case 3, for answers of 'yes' or 'no' in place of comparisons. The term:

$$\sqrt{\left(\frac{1}{A_1} + \frac{1}{A_2}\right) V}$$

can be regarded as the standard deviation of the distribution of $[(r + \Delta r) - r]$, assuming the two terms to be uncorrelated, and will be further referred to as σ_r. The constant will be called b.

Marriott[4] has shown that this equation leads to rather implausible consequences: (1) Although when the threshold is defined by a criterion such as 80 per cent of positive responses, ΔI will decrease as the area increases (causing σ_r to decrease), as Gregory[1] found, this will not be true when the criterion is 50 per cent positive responses, in which case threshold will be independent of changes in area. (2) With a criterion such as 20 per cent, ΔI decreases as the area decreases (σ_r increases). It might be added (3) that though the threshold will stay constant despite changes in area with a 50 per cent criterion, the false positive rate will decrease as the area increases. Consequently, Marriott rejects the approximations to Ricco's and Piper's laws for areal summation at the absolute threshold which Cane and Gregory derive from their assumptions.

The modification of the equation in a way suggested by the theory of signal detectability appears capable of avoiding these difficulties. In place of Gregory's assumption that a fixed difference between impulse-rates (or whatever central effects of the stimuli determine the responses) is required by the brain to establish discrimination, let us suppose that the discrimination mechanism operates to give maximum detection consistent with a limiting rate of false positive responses. In this case the value of C will not be constant, but must be defined as a function of σ_r. Let us therefore replace it by $m\sigma_r$, where the value of m determines the proportion of false positives. Thus, when $m = 2$, the false positive rate would be approximately equal to 2·5 per cent. The equation for the threshold can now be expressed as:

$$[(r + \Delta r) - r] = (m + b)\sigma_r \qquad (2)$$

Assuming that the distribution of $[(r + \Delta r) - r]$ is approximately normal, b is the normal deviate corresponding to the frequency of response required to define the threshold. When this is 50 per cent, $b = 0$ and the right-hand terms reduce to $m\sigma_r$. Thus the threshold is still directly proportional to σ_r, so that it will vary with area just as when it is defined by an 80 per cent requirement. This meets Marriott's first point. When the requirement is 20 per cent, the equation becomes $(r + \Delta r) - r = (m - b)\sigma_r$, where b is the normal deviate corresponding to 80 per cent negative responses. In this case too the threshold will decrease as σ_r decreases, that is, as the area increases, thus meeting the second objection. Moreover, so long as the response-rate required to define the threshold exceeds the false positive rate, $(m - b)$ will be positive.

Even though the threshold equation in the form above meets Marriott's objections, there is still reason to doubt the derivation of Ricco's and Piper's laws, based on the assumption that r is proportional to $\log(I + k)$, which is offered by Cane and Gregory, where k is a constant assumed by Gregory to represent the internal noise of the system. A very similar result is given by equation (2) to that obtained by Cane and Gregory with equation (1). At the absolute threshold, where $I = 0$, taking exponents in equation (2), and ignoring A_2, which is the total visual field, we get:

$$1 + \frac{\Delta I}{k} = e^{(m+b)(1/2)A^{-1/2}} \qquad (3)$$

Defining the unit of I so that $k = 1$, and putting $(m + b)(1/2) = d$, we get for the absolute threshold:

$$\Delta I = dA^{-1/2} + d^2/2A + d^3/6A^{3/2} \ldots \qquad (4)$$

Cane and Gregory obtain Ricco's law by multiplying throughout by A, and Piper's law by multiplying by $A^{1/2}$. In each case a constant appears among the terms on the right. However, it has been pointed out to me by Dr. Marriott (private communication) that in the first case it is the second term (as given in equation (4)) which provides the constant and in the second case the first term. This causes the following difficulty: the values of the terms on the right depend on the values of both d and A. While d and A can have values such that the first term is considerably larger than any other term, and decrease in the value of A will increase the size of the second term relative to the first term, it will cause the values of other terms to increase as well, and at no time will the second term be more than a fraction of the total value of ΔI (for example, if $d = 1$, $A = 10$, the first terms are 0·3, 0·05, 0·005. . . . If A is made 0·1, the terms are 3·2, 5·0, 5·3 . . .). Thus the unmodified assumption of a simple logarithmic transformation of the stimulus, so far from leading to Ricco's law, appears to exclude it.

I wish to thank Prof. R. C. Oldfield for research facilities, and Dr. C. I. Howarth and Dr. F. H. C. Marriott for helpful discussions.

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SOCIOLOGY

Conflicting Hypotheses on the Growth of World Population

Over the past twenty thousand years, the logarithm of human population of small areas such as England and Wales—when plotted against time—shows two or more special upsurges, or kinks; for example, due to the introduction of agriculture, or since A.D. 1500. One may recognize three main demographic stages[1]. With the same idea, Prof. E. S. Deevey of Yale proposes a striking plot of total world population, featuring two such kinks in a very pronounced manner[2]. But the "overall geographical speed of cultural diffusion", in early times, was slow; often between 0·5 and 5 km. per annum[3]. Consequently different small areas had their main kinks at widely different times; and they will practically disappear on summation. Hence, with due allowance for the different scales used, the relatively smooth curve for world population[4] seems likely to be much nearer the truth than Deevey's of the following September.

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FORTHCOMING EVENTS

(Meeting marked with an asterisk • is open to the public)

Monday, March 27

BRITISH INSTITUTION OF RADIO ENGINEERS, MEDICAL ELECTRONICS GROUP (at the Postgraduate Medical School, University of London, Hammersmith, London, W.12), at 3 p.m.—Symposium on "Electronic Instrumentation for Cardiac Surgery".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Mr. G. de Q. Robin : "The Antarctic Ice Sheet".•

INSTITUTION OF MECHANICAL ENGINEERS, INTERNAL COMBUSTION ENGINES GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Is Fuel-Injection Equipment Standardization Limiting the Development of Small Diesel Engines?".

OPERATIONAL RESEARCH SOCIETY (in the Lecture Theatre of the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Mr. D. T. Steer : "Feasibility and Financial Studies of a Port Installation".

Monday, March 27—Wednesday, March 29

BIOCHEMICAL SOCIETY (in London)—Fiftieth Anniversary Meeting.

Monday, March 27—Tuesday, March 28

(In the Senate House, University of London, W.C.1)—Symposium on "Structure and Synthesis of Macromolecules".

Tuesday, March 28

(At the Royal Institution, Albemarle Street, London, W.1)—Sir Hans Krebs : "The Physiological Role of Ketone Bodies" (Third Hopkins Memorial Lecture).

Wednesday, March 29

(At University College, Gower Street, London, W.C.1)—Original Communications and Annual General Meeting.

Tuesday, March 28

SOCIETY OF INSTRUMENT TECHNOLOGY, CONTROL SECTION (at 26 Portland Place, London, W.1), at 5 p.m.—Dr. P. E. W. Grensted and Mr. O. L. R. Jacobs : "Automatic Optimization". 7 p.m.—Mr. P. F. Sutherby : "The Development of an Optimizing Controller".

ROYAL SOCIETY OF MEDICINE, MEDICINE SECTION (at 1 Wimpole Street, London, W.1), at 8 p.m.—Meeting on "Isotopes in Medicine". Speakers : Prof. G. M. Wilson, Prof. D. W. Smithers and Dr. E. Williams.

Tuesday, March 28—Thursday, March 30

ROYAL INSTITUTION OF NAVAL ARCHITECTS (in the Weir Lecture Hall, 10 Upper Belgrave Street, London, S.W.1), at 10.15 a.m. daily—Spring Meeting.

Wednesday, March 29

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 3 p.m.—Symposium on "Electronic Instrumentation for Nuclear Power Stations".

INSTITUTION OF MECHANICAL ENGINEERS (in conjunction with the STEAM PLANT GROUP, at 1 Birdcage Walk, Westminster, London, S.W.1), at 3.30 p.m.—Mr. R. W. Haywood, Mr. C. A. Knights, Mr. C. E. Middleton and Mr. J. R. S. Thom: "An Experimental Study of the Flow Conditions and Pressure Drop of Steam-Water Mixtures at High Pressures in Heated and Unheated Tubes".

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Chelsea College of Technology, Manresa Road, Chelsea, London, S.W.3), at 6 p.m.—Demonstration of Laboratory-Made Equipment".

ROYAL AERONAUTICAL SOCIETY, AGRICULTURAL AVIATION GROUP (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. R. P. Fraser : "Atomization".

ROYAL INSTITUTE OF CHEMISTRY (at Hendon Technical College, The Burroughs, London, N.W.4), at 7.30 p.m.—Dr. K. G. A. Pankhurst: "The Story of Soap and the Growth of Modern Synthetic Detergents".•

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned :

SENIOR RESEARCH ASSISTANT (postdoctoral standard, qualified in inorganic chemistry), to take part in an investigation of the crystal chemistry of oxides and hydroxides of the transition metals—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (April 5).

RESEARCH FELLOW (with a first degree in biochemistry, chemistry or botany, and research experience in biochemistry and particularly in the use of radioactive tracers) IN PLANT BIOCHEMISTRY in the Department of Botany, to participate in research on the mechanism of photosynthesis—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (April 7).

LECTURER OR ASSISTANT LECTURER IN ZOOLOGY—The Secretary, The University, Exeter (April 10).

ZOOLOGY ASSISTANT (Grade B) (with good academic qualifications) IN THE DEPARTMENT OF BOTANY AND ZOOLOGY—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (April 10).

ASSISTANT IN PHYSICAL OR INORGANIC CHEMISTRY—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (April 15).

CHAIR OF AGRICULTURE; CHAIR OF PHYSICS; CHAIR OF EDUCATION; and CHAIR OF GEOGRAPHY—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas (Dept. T.1), 29 Woburn Square, London, W.C.1 (April 15).

LECTURER IN MICROBIOLOGY; and a LECTURER OR ASSISTANT LECTURER IN PHARMACOLOGY at the University College of the West Indies—The Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1 (April 17).

CHAIR OF ZOOLOGY tenable in the Durham Division of the University—The Registrar, University Office, 40 North Bailey, Durham (April 22).

ORGANIC CHEMIST (graduate, or holder of a technical college diploma majoring in organic chemistry, and preferably with experience of distillation and chromatographic techniques) IN THE DIVISION OF COAL RESEARCH, C.S.I.R.O., Sydney, Australia, to assist on investigations of the chemical constitution of coal tar and pitch and in the development of new industrial uses for these materials—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 480/359 (April 22).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN BIOCHEMISTRY, CHEMISTRY, CHEMOTHERAPY, ENGINEERING, METALLURGY, PHARMACOLOGY OR PHYSICS—The Academic Registrar, University of London, Senate House, London, W.C.1 (April 25).

LECTURER IN MATHEMATICS at the University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 25).

SENIOR LECTURER IN PHYSICS; a SENIOR LECTURER (graduate with Corporate Membership of the Institution of Electrical Engineers) IN ELECTRICAL ENGINEERING; a LECTURER IN BOTANY; a LECTURER OR ASSISTANT LECTURER (preferably with qualifications in physical and/or inorganic chemistry) IN CHEMISTRY; and a LECTURER (preferably with qualifications and/or experience in palæontology, stratigraphy or structural physical geology) IN GEOLOGY, at the Royal College, Nairobi—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 25).

ASSISTANT LECTURER (honours graduate) IN PHYSIOLOGY; and an ASSISTANT LECTURER (honours graduate) IN BIOCHEMISTRY—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (April 28).

LECTURER IN PHILOSOPHY at the University of New England, Armidale, New South Wales, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 28).

SENIOR LECTURER/LECTURER (preferably with previous research experience) IN THE DEPARTMENT OF STATISTICS of the School of Mathematics, University of New South Wales, Kensington—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 (Australia and London, April 30).

BURN RESEARCH FELLOW (graduate, not less than thirty years old, with two or three years research experience) IN PHARMACOLOGY at Oxford—Secretary to the Trustees, Department of Pharmacology, University of Oxford (May 15).

LECTURER OR SENIOR LECTURER IN MATHEMATICS at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 15).

CHAIR OF AGRICULTURE in the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 31).

MCCAUGHEY CHAIR OF GEOGRAPHY in the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 31).

ASSISTANT LECTURER (preferably with research experience in some field of experimental zoology) IN THE DEPARTMENT OF BIOLOGY AS APPLIED TO MEDICINE—The Secretary, Department of Biology as Applied to Medicine, Middlesex Hospital Medical School, London, W.1 (July 1).

LECTURER and an ASSISTANT LECTURER IN THE DEPARTMENT OF ANATOMY—The Secretary, University College London, Gower Street, London, W.C.1.

MASTER TO TEACH MATHEMATICS to G.C.E. "O" level—The Headmaster, Queen Elizabeth's Grammar School, Blackburn.

READER, and a LECTURER, IN LOW TEMPERATURE PHYSICS—The Clerk to the Governing Body, Battersea College of Technology, London, S.W.11.

RESEARCH ASSISTANTS (with a degree in chemistry or chemical engineering, or with equivalent qualifications such as Grad.R.I.C.) IN THE DEPARTMENT OF CHEMISTRY, for experimental work on the thermodynamic properties of gases and of liquid mixtures—The Bursar, The University, Reading.

RESEARCH CHEMIST (with experience of research work in physical chemistry or chemical engineering, and preferably with a higher degree in one of these subjects) IN THE DEPARTMENT OF CHEMISTRY to continue a study of the thermodynamics of imperfect gases, under the items of a contract between the University and the D.S.I.R.—The Registrar (Room 22 O.R.B.), The University, Reading.

RESEARCH CONSULTANT (with sound British academic qualifications, and specialized in physical or inorganic chemistry) IN THE CENTRE OF CHEMISTRY at the University of Chile, Santiago, to conduct and advise on research, advise on the organization of the Centre, and to conduct courses for the research staff—The Director, Recruitment Department, The British Council, 65 Davies Street, London, W.1, quoting Ref. N.4.T(61).

WHOLE-TIME BIOCHEMIST (non-resident), for hospital biochemical work in the Mansfield Area Pathology Service—The Hospital Secretary, King's Mill Hospital, Sutton-in-Ashfield, Notts.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Organometallic Compounds. No. 1. A new abstract journal. Published monthly. Subscription rates: £6 per year U.K. and Overseas. Airmail postage Overseas £9. United States and Canada 18 dollars seamail, 27 dollars airmail. Pp. 1+25. (London: Translation and Technical Information Services, 32 Manaton Road, S.E.15, 1961.) [2012

Ministry of Labour. Health at Work: a Description of Medical Services in Fourteen British Factories. Pp. 76. (London: Ministry of Labour, 1960.) [2012

Colonial Office. Colonial Research Studies No. 31: The Insect Pests of Graminaceous Crops in East Africa—Report of a Survey carried out between March 1956 and April 1959. By I. W. B. Nye. Pp. iii+48. (London: H.M. Stationery Office, 1960.) 10*s.* 6*d.* net. [2012

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 10: Apple Capsids. Pp. 4. Leaflet No. 89: Some Pests and Diseases of Vegetable Crops. Pp. 13. (Belfast: Ministry of Agriculture, 1960.) [2012

Agricultural Research Institute of Northern Ireland. Thirty-third Annual Report, 1959-1960. Pp. 47. (Hillsborough, Co. Down: Agricultural Research Institute of Northern Ireland, 1960.) [2012

The Institute of Physics and the Physical Society. Handbook of Scientific Instruments and Apparatus, 1961 Exhibition. Pp. xvi+335+A75. (London: Institute of Physics and the Physical Society, 1960.) [2012

Department of Scientific and Industrial Research. Research and Development Requirements of the Shipbuilding and Marine Engineering Industries. Pp. vi+18. (London: H.M. Stationery Office, 1960.) 1*s.* 6*d.* net. [2012

Tweed River Purification Board. Annual Report for the year ended 15th May, 1960. Pp. 39. (Newton St. Boswells: Tweed River Purification Board, 1960.) [2012

Privy Council. Medical Research Council Special Report Series, No. 297: The Composition of Foods. By Dr. R. A. McCance and Dr. E. N. Widdowson. (Third revised edition of Special Report No. 235). Pp. viii+252. (London: H.M. Stationery Office, 1960.) 30*s.* net. [2012

University Grants Committee. Methods used by Universities of Contracting and of Recording and Controlling Expenditure. Pp. 28. (Cmnd. 1235). (London: H.M. Stationery Office, 1960.) 1*s.* 6*d.* net. [2212

Ministry of Transport. Reorganization of the Nationalized Transport Undertakings. Pp. 14. (Cmnd. 1248). (London: H.M. Stationery Office, 1960.) 1*s.* net. [2212

Medical Research Council. The Hazards to Man of Nuclear and Allied Radiations—a Second Report to the Medical Research Council. Pp. vii+154. (Cmnd. 1225). (London: H.M. Stationery Office, 1960.) 7*s.* net. [3012

General Register Office. The Registrar General's quarterly return for England and Wales—Births, Deaths and Marriages; Infectious Diseases; Weather; Population Estimates: quarter ended 30th September 1960, 3rd quarter, 1960, No. 447. Pp. 20. (London: H.M. Stationery Office, 1960.) 2*s.* net. [3012

Other Countries

National Science Foundation. Scientific and Technical Personnel in American Industry: Report on a 1959 Survey. Pp. vi+66. (Washington, D.C.: Government Printing Office, 1960.) 45 cents. [2012

Mitteilungen aus der Biologischen Bundesanstalt für Land—und Forstwirtschaft, Berlin-Dahlem. Heft 100 (Oktober 1960): Das Trichogramma-Problem. Pp. 50 (4 tafel). (Berlin-Dahlem: Biologische Bundesanstalt für Land—und Forstwirtschaft, 1960.) 9.60 D.M. [2012

Carnegie Institution of Washington. The Report of the President, 1959-1960. Pp. xiii-lxxiv. (Reprinted from *Carnegie Institution of Washington Year Book*, for the year 1959-1960.) (Washington, D.C.: Smithsonian Institution, 1960.) [2012

United Nations Educational, Scientific and Cultural Organization. Centro de Cooperacion Cientifica para America Latina. Scientific Institutions and Scientists in Latin-America. Argentina—(Cientificos), N-Z. (IV Volumen) Fasciculo IV. Pp. 453-706. (Montevideo: UNESCO, Centro de Cooperacion Cientifica para America Latina, 1960.) [2012

Trinidad and Tobago. Administrative Report of the Forest Department for the year 1958. Pp. 35. (Trinidad, W.I.: Government Printing Office, 1960.) [2012

United States Department of the Interior: Fish and Wildlife Service. Statistical Digest No. 45: Alaska Fishery and Fur-Seal Industries, 1958. By Seton H. Thompson and Donald W. Erickson. Pp. v+88. (Washington, D.C.: Government Printing Office, 1960.) 40 cents. [2012

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 41 (October, 1960): Company Award for Research in Accident Prevention. Growth Trends in the Teen Ages. Causes of Death in Later Life. Accidental Fires in the Home. Pp. 12. (New York: Metropolitan Life Insurance Company, 1960.) [2012

United States Department of Commerce: Coast and Geodetic Survey. Publication 65-1, Part 13: Plane Coordinate Intersection Tables (2½-minute), Iowa. Pp. iii+91. (Washington, D.C.: Government Printing Office, 1960.) 50 cents. [2012

Companhia de Diamantes de Angola (DIAMANG). Servicos Culturais. Dundo-Lunda-Angola. Museu do Dundo. Publicacoes Culturais No. 51: Subsidios para o Estudo da Biologia na Lunda—Estudos Diversos (XIX). Pp. 186. (Lisboa: Companhia de Diamantes de Angola, 1960.) [2012

United States Department of the Interior: Geological Survey. Bulletin 1072-N: Stratigraphy of the Little Rocky Mountains and Encircling Foothills, Montana. By Maxwell M. Knechtel. Pp. iv+723-752+plates 52 and 53. Bulletin 1072-P: Coal Resources of Arkansas, 1954. By Boyd R. Haley. Pp. iv+795-831+plates 58-64. Bulletin 1087-F: Geology and Ore Deposits of the Kern River Uranium Area, California. By E. M. MacKevett, Jr. Pp. iv+169-222+plates 19-25. Bulletin 1087-H: Geology of the Clay Hills Area, San Juan County, Utah. By Thomas E. Mullens. Pp. iv+259-336+plate 27. 75 cents. Bulletin 1096-A: Geology of the Grosvenor Quadrangle, Brown and Coleman Counties, Texas. By Robert T. Terriere. Pp. iv+35+plates 1-3. Bulletin 1072-J: Reconnaissance Geology of the Birney-Broadus Coal Field, Rosebud and Powder River Counties, Montana. By W. C. Warren. Pp. iv+561-585+plates 19-26. (Washington, D.C.: Government Printing Office, 1959 and 1960.) [2012.

United States Department of the Interior: Geological Survey. Water-Supply Paper 1455-A: Floods of May 1955 in Colorado and New Mexico. By Walter C. Vaudrey. Pp. vii+68+plates 1-4. Water-Supply Paper 1459-G: Iron Content of Selected Water and Land Plants. By Eugene T. Oborn. Pp. iii+191-211+plate 1. Water-Supply Paper 1460-H: Ground-Water Problems in the Vicinity of Moscow, Latah County, Idaho. By P. R. Stevens. Pp. iv+325-357+plate 13. Water-Supply Paper 1482: Geology and Ground-Water Resources of the Gallatin Valley, Gallatin County, Montana. By O. M. Hackett, F. N. Visher, R. G. McMurtrey, and W. L. Steinhilber. Pp. viii+282+11 plates. Water-Supply Paper 1464: Geology, Water-Resources and Useable Ground-Water Storage Capacity of Part of Solano County, California. By H. G. Thomasson, Jr., F. H. Olmsted, and E. F. LeRoux. Pp. x+693+23 plates. (Washington, D.C.: Government Printing Office, 1960.) [2012

United States Department of the Interior: Geological Survey. Water-Supply Paper 1623: Surface Water Supply of the United States 1959. Part 2-A: South Atlantic Slope Basins, James River to Savannah River. Prepared under the direction of J. V. B. Wells. Pp. viii+267. 1 dollar. Water-Supply Paper 1626: Surface Water Supply of the United States 1959. Part 3-B: Cumberland and Tennessee River Basins. Prepared under the direction of J. V. B. Wells. Pp. vii+242. 1 dollar. Water-Supply Paper 1637: Surface Water Supply of the United States 1959. Part 13: Snake River Basin. Prepared under the direction of J. V. B. Wells. Pp. ix+271. Water-Supply Paper 1638: Surface Water Supply of the United States 1959. Part 14: Pacific Slope Basins in Oregon and Lower Columbia River Basin. Prepared under the direction of J. V. B. Wells. Pp. ix+300. 1 dollar. (Washington, D.C.: Government Printing Office, 1960.) [2012

United States Department of the Interior: Geological Survey. Professional Paper No. 296: Geology of Glacier National Park and the Flathead Region, Northwestern Montana. By Clyde P. Ross. Pp. iv+125+plates 1-4. Professional Paper 329: Reconnaissance of the Geomorphology and Glacial Geology of the San Joaquin Basin, Sierra Nevada, California. By Francois E. Matthes. Pp. vi+62+2 plates. Professional Paper 334-E: Upper Cretaceous Pelecypods of the Genus Inoceramus from Northern Alaska. By David L. Jones and George Gryc. Pp. iii+149-165+plates 15-23. 45 cents. Professional Paper 343: Geology and Ore Deposits of the Summitville District, San Juan Mountains, Colorado. By Thomas A. Steven and James C. Ratté. Pp. iv+70+plates 1-9. 2 dollars. Professional Paper 355: Studies of Mowry Shale (Cretaceous) and Contemporary Formations in the United States and Canada. By John B. Reeside, Jr., and William A. Cobban. Pp. iv+126+58 plates. Professional Paper 400-A: Geological Survey Research 1960: Synopsis of Geologic Results. Pp. xii+136. 1 dollar. (Washington, D.C.: Government Printing Office, 1960.) [2012

United States Department of Agriculture. Home and Garden Bulletin No. 75: The European Earwig—How to Control It Around the Home. Pp. 8. (Washington, D.C.: Government Printing Office, 1960.) 5 cents. [3012

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Western Nigeria. Annual Report on the Forest Administration of the Western Region of Nigeria for the year 1958-59. Pp. iii+43. (Ibadan: Government Printer, 1960.) 1*s.* [3012

Indian Forest Records (New Series). Forest Pathology, Vol. 2, No. 5: Root Diseases of Shisham (*Dalbergia sissoo* Roxb.). 8: Inoculation Studies on Wilt. By B. K. Bakshi and Sujan Singh. Pp. ii+71-76+3 plates. Rs. 3.30nP.; 6*s.* 6*d.* Mycology, Vol. 1, No. 10: List of Common Names of Fungi Attacking Indian Forest Trees, Timber and Herbaceous and Shrubby Undergrowths, and List of Cultures of Forest Fungi. By K. Bagchee and Ujagar Singh. Pp. ii+199-348. Rs. 11.50nP.; 18*s.* (Delhi: Manager of Publications, 1960.) [3012

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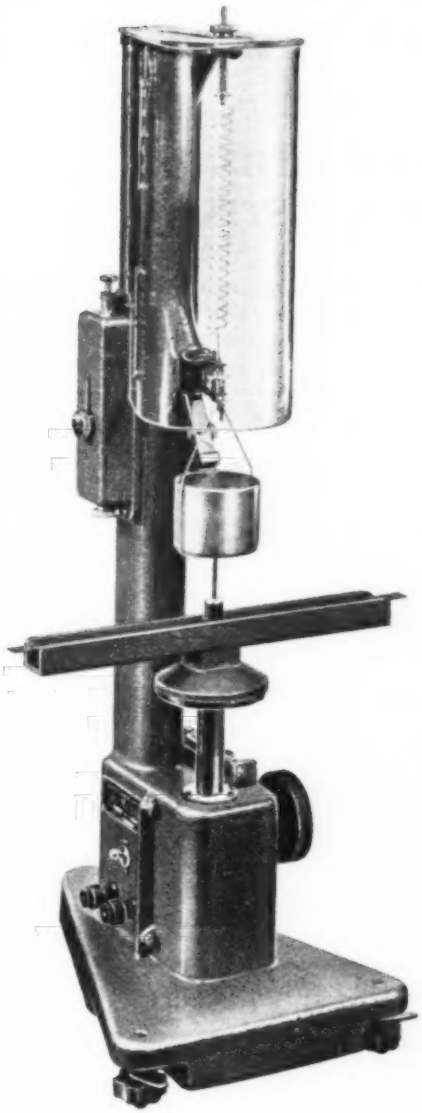

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W. L. CHINN,
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UNIVERSITY OF DURHAM

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GOWER STREET, W.C.1
DEPARTMENT OF CHEMICAL ENGINEERING

Research Assistant required for work on the fractionation and analysis of lipoprotein extracts. Salary about £700 per annum. No specialized experience necessary, but good chemical background desirable.

Applications should be sent to the Secretary, from whom further particulars may be obtained.

ANIMAL HEALTH TRUST

Bacteriologist, graduate in science or veterinary science, required to assist in a programme of research into enteric diseases of young farm animals, with especial reference to pigs, at the Animal Health Trust, Farm Livestock Research Centre, Stock, Essex. Salary within the scale £650 by £30 to £1,100; point of entry to be determined by age and experience. The post is superannuated under the F.S.S.U.

Further particulars can be obtained from the Scientific Director, Animal Health Trust, 14 Ashley Place, London, S.W.1, to whom applications should be addressed.

BELFAST EDUCATION COMMITTEE
COLLEGE OF TECHNOLOGY

Principal: D. H. Alexander, O.B.E., F.C.G.I., M.Sc., Wh.Sch., M.I.Mech.E.

Applications are invited for the position of HEAD OF THE DEPARTMENT OF TEXTILE INDUSTRIES in the College of Technology, Belfast.

Though chiefly concerned with flax and linen, the department is also equipped to deal with the study of other natural and synthetic fibres, and is now being reorganized to meet the needs of the modern textile industry. The person appointed will be required to advise on this reorganization and to assist in carrying it out. He will also be expected to work in close contact with local industry, and will be given facilities for carrying out research and consulting work. Applicants should have had a scientific training to graduate level, not necessarily in textile technology, but possibly in engineering or physics. They should also have experience in industry. An otherwise suitable candidate, with insufficient experience in the field of textiles, may be given assistance to enable him to spend some time in textile works or research establishments. The present salary attached to the position is £1,600 per annum, rising by annual increments of £50 to £1,800 per annum, and approved service elsewhere will be taken into account in fixing the commencing salary.

Application form and full particulars may be obtained from the Principal, College of Technology, Belfast 1, with whom applications should be lodged not later than Saturday, April 8, 1961. Canvassing is strictly forbidden and will disqualify.

J. STUART HAWNT,
Director of Education.

COLUMBIA UNIVERSITY
RESEARCH APPOINTMENTS IN X-RAY CRYSTALLOGRAPHY

Applications are invited for two post-doctoral appointments in X-ray Crystallography in the Department of Biochemistry. The principal research problems under investigation are the crystal structure analyses of the protein hormone insulin and the peptide hormone oxytocin. One of these appointments is open to candidates with special interests in computing methods and in the computing problems associated with the determination of the structure of large molecules. Some previous experience in computer programming would be an advantage. The appointee will work initially with a member of the research group experienced in this field. Computational facilities, IBM 650, 709 and 7090 are available. Candidates for both appointments should have a doctoral degree, or its equivalent in experience, and have undertaken research in single crystal structure determination. Opportunities will be available to candidates with an interest in teaching X-ray crystallography. The salary offered will be determined by qualifications and experience. The appointments are for a minimum period of two years.

Applications and requests for further information should be sent to Dr. Barbara W. Low, Department of Biochemistry, College of Physicians and Surgeons, 630 West 168th Street, New York 32, N.Y.

UNIVERSITY OF WESTERN ONTARIO
LONDON, CANADA

Applications are invited for two appointments to the staff of the Department of Mathematics. Full qualifications include Ph.D. degree in mathematics. Algebraist and analyst preferred. Initial appointments with the rank of Assistant Professor, effective July 1, 1961, teaching duties to commence in September. Life and hospitalization insurance effective at beginning of teaching duties. Pension plan entered after two-year probationary period. Also available four Teaching Fellowships for graduate study in mathematics.

Address applications with two references to Department of Pure and Applied Mathematics, University of Western Ontario, London, Canada.

UNIVERSITY OF READING
DEPARTMENT OF CHEMISTRY

Applications are invited for one or more Research Assistantships for experimental work on the thermodynamic properties of gases and of liquid mixtures. Candidates should have a degree in chemistry or chemical engineering or should have equivalent qualifications such as Grad.R.I.C. The commencing salary will be not less than £475 per annum depending on age and experience. Research Assistant will be able to apply to register for a higher degree.

Applications should be sent as soon as possible to the Bursar, the University, Reading.

NEW ZEALAND
EDUCATION DEPARTMENT

Applications are invited for the following positions at the New Zealand School of Pharmacy:

SENIOR TUTOR OR TUTOR IN PHARMACEUTICS

Applicants should possess a degree or registrable qualification in pharmacy and have had teaching experience. A postgraduate qualification and/or research experience would be an additional advantage.

The appointee will be in charge of all the teaching in pharmaceutics and will be particularly responsible for the teaching of pharmaceutical microbiology.

TUTOR OR ASSISTANT TUTOR IN PHARMACOGNOSY

Applicants should possess a degree or registrable qualification in pharmacy. A postgraduate qualification, teaching or research experience would be an additional advantage. The appointee will be responsible for all the teaching in Pharmacognosy and should also be prepared to assist with the teaching of pharmaceutics.

SENIOR TUTOR OR TUTOR IN PHARMACEUTICAL CHEMISTRY

Applicants should possess a degree or registrable qualification in pharmacy and should preferably have had teaching experience. The ability to teach pharmacology would be an additional advantage.

Salary (operative from April 1, 1961):
Senior Tutor in the range £1,515 to £1,705.
Tutor in the range £1,260 to £1,515.
Assistant Tutor in the range £910 to £1,260.

The scales apply to both male and female staff and the commencing salary will depend on qualifications and experience.

Passages: Steamer fares of up to £165 each for the appointee and his wife, and pro rata for dependent children will be paid.

Incidental expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Inquiries quoting reference number B11/8/9 should be addressed to the High Commissioner for New Zealand, 415 Strand, London, W.C.2, who will supply further details and application forms.

Completed applications to be lodged with his office not later than April 10, 1961.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

The Department of Electrical Engineering has vacancies for Lecturers in fields including: (i) electrical machines; (ii) electric traction; (iii) automatic control—mathematical aspects; (iv) electron physics—vacuum and plasma devices. The Department is soon to occupy a new building with modern equipment, and research is in progress in all these fields. Candidates will, in general, be expected to participate in postgraduate teaching and research. Salaries in scale £1,050 by £50 to £1,400 by £75 to £1,550 (bar) by £75 to £1,850, plus £60 per annum London allowance, family allowances and F.S.S.U. membership. Some appointments may be made in higher part of range, in the case of suitably qualified candidates.

Apply to Head of Department of Electrical Engineering, Imperial College of Science and Technology, London, S.W.7.

THE LONDON HOSPITAL, WHITECHAPEL, E.1, has vacancy in their Physics Department for a Physicist in the Senior Grade. Applicants should have an honours degree in physics and previous experience in radiation physics. Duties will include problems arising in radiotherapy as well as helping to run the hospital and regional film badge services (a full-time technician is available for these). There are good opportunities for development and research and technical assistance includes a first-class instrument workshop. Salary: £1,300 to £1,750 per annum.—Applications with the names of two referees to the House Governor by April 5.

UNIVERSITY OF READING
DEPARTMENT OF CHEMISTRY

Applications are invited for a Research Chemist to continue a study of the thermodynamics of imperfect gases under the terms of a contract between the University and the D.S.I.R. Candidates should have experience of research work in physical chemistry or chemical engineering and should preferably have taken a higher degree in one of these subjects. The appointment will be for one year in the first instance (from a date to be arranged) but is likely to be renewed for two further years. The commencing salary will be not less than £800 per annum depending on the qualifications and experience of the successful applicant.

Applications, including names of not more than three referees, should be sent as soon as possible to the Registrar (Room 22, O.R.B.), the University, Reading.

CENTRAL ELECTRICITY GENERATING BOARD

ASSISTANT LIBRARIAN

required in the Board's Central Library at Headquarters, Bankside House, London, S.E.1.

The Library provides a service to all sections of the Electricity Supply Industry throughout the country and has a stock of some 30,000 items, with a regular intake of 700 periodicals.

The successful candidate will be required to take charge of a group responsible for handling internal and inter-library loans, at present about 30,000 per annum, and the circulation of periodicals. There are five junior staff in this group. In addition, the Assistant Librarian will be required to help with cataloguing and classification, and the organization of the library generally. There will also be a responsibility for supervising the training of junior staff to satisfy Library Association requirements.

Applicants should, therefore, be Chartered Librarians, preferably with experience in a special library.

Salary within the range £935 to £1,060 per annum.

Applications, stating age, qualifications, experience, present position and salary, should be forwarded to the Appointments Officer, 24/30 Holborn, London, E.C.1, to arrive not later than April 5. Applications should be marked "Confidential. Ref. N.132."

AUSTRALIAN NATIONAL UNIVERSITY
INSTITUTE OF ADVANCED STUDIES JOHN CURTIN SCHOOL OF MEDICAL RESEARCH
RESEARCH FELLOWSHIP IN PHYSICAL BIOCHEMISTRY

Applications are invited for a Research Fellowship in the Department of Physical Biochemistry. Research experience in biochemistry or chemistry and interest in physico-chemical aspects of biochemistry are essential. The Research Fellow will be allowed reasonable scope in the choice of his research. The salary range for Research Fellows is £A.1,437 to £A.2,152, with increments of £A.65 per annum, but this range is under review; initial salary will depend on qualifications and experience. Appointment is for three years, with possible extension to a maximum of five years. Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid and assistance with housing is provided. A summary of the conditions of appointment is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on April 28, 1961.

Details of the research being carried out may be obtained from the Head of the Department, Professor A. G. Ogston, F.R.S.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Assistant Lecturer in Inorganic Chemistry. Salary on a scale £800 to £950 per annum, with membership of the F.S.S.U. and children's allowance scheme.

Applications should be sent not later than April 15, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

THE PATENT OFFICE
OFFERS SCIENTISTS A CAREER WITH AN ASSURED FUTURE

SALARY. Starting salary within the scale £793 to £1,719 according to experience, with advances in the scale to £941 after two years and to £1,324 after 3 to 5 years, for those starting below these points. One promotion only (prospects excellent) raises maximum to £2,715. Further prospects up to £4,415.

QUALIFICATIONS. Age 21 to 36 and Degree or Diploma of Technology with first- or second-class honours in physics, chemistry, engineering or mathematics, or equivalent professional qualification, e.g., A.Inst.P., A.R.I.C., or corporate membership of I.C.E., I.Mech.E. or I.E.E.

INTEREST. The examination of patent specifications will maintain your knowledge of science and technology completely up-to-date and will give you inside knowledge of new manufactures well ahead of the public at large.

CONDITIONS. Location, London. Five-day week. Annual leave 4½ rising to 6 weeks with considerable freedom as to when it is utilized. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information or for a visit to see the work. *The Superintending Examiner (B. Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Holborn 8721, Ext. 324.*

RUBBER RESEARCH INSTITUTE OF MALAYA

The Board of the Rubber Research Institute invites applications from Biochemists for the post of Research Officer, Division A, in the Chemical Division of the Institute at Kuala Lumpur. The successful candidate must possess an honours degree and have two years' post-graduate research experience in biochemistry or phytochemistry. Preference will be given to candidates who have already established themselves as investigators in the field of biochemical research. The successful candidate will work on problems connected with the biosynthesis of rubber. The basic salary of the appointment will be within the scale £1,400 by £70 to £2,660 per annum, plus other allowances ranging from £140 to £630 per annum, depending on country of domicile. An employee of overseas domicile is provided with rent-free quarters and an additional allowance towards the education of children ranging from £140 to £420 per annum. There is a contributory Provident Fund.

Application forms and further particulars of the post may be obtained from the Secretary, Natural Rubber Bureau, Commonwealth Institute, Imperial Institute Road, London, S.W.7. The closing date for applications is May 5, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for an Assistantship in Physical or Inorganic Chemistry in the Department of Chemistry, Queen's College, Dundee, commencing October 1, 1961. Salary scale: £800 by £50 to £950. Appointment for three years, with possibility of renewal for fourth and final year. F.S.S.U. Family allowance. Grant towards furniture removal expenses.

Applications (six copies), containing the names of three referees, to the undernoted not later than April 15, 1961.

PATRICK CUMMING,
Joint Clerk to the University Court.
Queen's College, Dundee.

KING'S COLLEGE HOSPITAL MEDICAL School has two vacancies for part-time Technicians. (i) To assist with simple culture preparation and histology in mycological research. (ii) To assist in the research work of the Department of Bacteriology. Salary according to experience.—Applications, stating age, qualifications and experience should be sent immediately to the Chief Technician, Department of Pathology, King's College Hospital Medical School, Denmark Hill, London, S.E.5.

Opportunity at Battelle

for

Fundamental Research in METALLURGY

Our programme of fundamental research in metallurgy is continuing to expand. Now we need a very high calibre man to conduct studies on: electronic bonding, defect structures, mechanisms of deformation and fracture in transition metals. He will also have ample time and support for research in areas of his choosing.

Required is a Ph.D. in Metallurgy with up to ten years' research experience at a university or in a fundamental research laboratory. . . . We offer world-renowned facilities and technical aid, competitive salary, full benefits programme.

Write: Mr. L. G. Hill,

BATTELLE MEMORIAL INSTITUTE
505 King Avenue
Columbus 1, Ohio, U.S.A.

UNIVERSITY OF MELBOURNE

CHAIR OF MATHEMATICS (R.A.A.F. ACADEMY)

Applications are invited for the above Chair. Duties will be mainly at the Royal Australian Air Force Academy, Point Cook, Victoria. The Professor will be a full-time officer of the University and will be expected to engage in research which will be promoted or pursued either in the University or in the Academy or in both places if appropriate. It is the expressed desire of both the University and the R.A.A.F. that there should be the freest possible interchange of facilities in this regard. The salary will be £A.4,000 per annum. Superannuation similar to F.S.S.U. in Great Britain will be provided.

Further particulars and conditions of appointment may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 15, 1961.

UNIVERSITY COLLEGE OF SWANSEA

DEPARTMENT OF BOTANY

Applications are invited for the following posts:

Research Demonstrator. Applicants should be graduates in Botany and will be expected to engage in research, preferably in plant physiology and biochemistry, plant pathology and ecology. Salary scale £650 to £700 per annum, together with F.S.S.U. benefits and family allowances.

Research Assistant. Applicants should be graduates in Botany or should graduate this year. The person appointed will assist the Professor in the establishment and maintenance of a Collection of plant organ and tissue cultures and in research involving these cultures. Salary in the range £500 to £650 per annum.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies), must be received not later than Saturday, May 13, 1961.

AUSTRALIA

UNIVERSITY OF NEW SOUTH WALES
SENIOR LECTURER/LECTURER IN THE SCHOOL OF MATHEMATICS

The University invites applications for appointment to the position of Senior Lecturer/Lecturer in the Department of Statistics of the School of Mathematics at Kensington. Salary: Lecturer, £A.1,766 range £A.2,471 per annum; Senior Lecturer, £A.2,586 range £A.3,036 per annum. Commencing salary according to qualifications and experience. Applicants for the position of Lecturer must possess a degree with honours in mathematics or equivalent qualifications: for appointment as Senior Lecturer applicants must possess a higher degree or equivalent qualifications. Previous research experience would be an advantage. Subject to passing a medical examination, appointee will be eligible to contribute to the State Superannuation Fund. First-class ship fares to Sydney of appointee and family will be paid. Appointee will be eligible for 12 months study leave on full salary after six years service.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded by air mail to the Appointments Section, The University of New South Wales, Box 1, P.O. Kensington, N.S.W., before April 30, 1961.

BRADFORD INSTITUTE OF TECHNOLOGY

The continued expansion of the work of the Institute, particularly in courses for the Diploma in Technology, has created additional vacancies in the various departments and applications are invited for the posts of:

Senior Lecturers in Mechanical Engineering, Mathematics, Physics, Chemical Engineering, Electrical Engineering, Pharmaceutics, Pharmacology, Pharmacognosy, Textile Physics.

Lecturers in Physical Chemistry, Mechanical Engineering, Mathematics, Physics, Chemical Engineering, Electrical Engineering, Pharmaceutics, Pharmaceutical Chemistry, Pharmacology, Pharmacognosy, Accounting, Economics, Government, History and Philosophy of Science, Production, Management, and Work Study.

Adequate facilities are given to undertake research, and suitable technical assistance and equipment are available. Staff are encouraged to develop industrial contacts and to undertake consultant work in industry and may retain fees paid for such work. Salary scales: Senior Lecturer, £1,550 to £1,750 per annum; Lecturer, £1,370 to £1,550 per annum. Previous industrial or research experience, at a suitable level, may be taken into account in fixing the commencing salary.

Further particulars and forms of application may be obtained from the Registrar (Department F), Bradford Institute of Technology, Bradford, 7.

HENRY PATTEN,
Clerk to the Governors.

UNIVERSITY OF LIVERPOOL

Applications are invited for the following posts in the School of Dental Surgery: (a) Assistant Lecturer or Lecturer in Dental Biochemistry at an initial salary within the range £800 to £1,475 per annum, according to age, qualifications and experience of the successful candidate. Applications stating age, qualifications and experience together with the names of three referees, should be received not later than April 30, 1961, by the Registrar, from whom further particulars may be obtained. Quoting reference CV/N. (b) Research Assistant in Dental Biochemistry to pursue investigations into the metabolism of bone and teeth. The appointment will commence in September, 1961, and will be for one year in the first instance, but renewable for a maximum period of two further years. The holder of the appointment will have the opportunity to read for a higher degree. Applicants should hold a good honours degree in biochemistry. The salary for the first year will be £500.

Applications, stating age, nationality, qualifications and experience, together with the names of two referees, should be received by the Registrar not later than June 30, 1961. Quoting reference CV/N.

LABORATORY TECHNICIAN (GRADE III) required for the Department of Physiological Chemistry to assist with classes in practical physiology and some experimental work. Salary scale £490 by £20 to £550 (bar) £600 by £25 to £675 with supplements of £30 or £25 per annum for appropriate qualifications.—Further particulars from the Assistant Bursar, the University, Reading.

"SCIENCE ABSTRACTS"

is increasing its

PHYSICS AND ELECTRICAL EDITORIAL STAFF

in response to the rising volume of world scientific literature. Its two monthly publications, "Physics Abstracts" and "Electrical Engineering Abstracts," are the largest British reference periodicals in their field, and are expanding at an average annual rate of nearly 10 per cent. The positions offered will suit those with an interest in the international literature of science and engineering, and a taste for concise writing and orderly arrangement. Applicants should have a good basic knowledge of their subject (honours degree, Graduate I.E.E. or equivalent); other qualifications (languages, specialized experience) will receive due recognition. Commencing salary within the range £800 to £1,200, according to age, qualifications and experience. Contributory Pension Scheme.

Apply: The Institution of Electrical Engineers, Savoy Place, W.C.2 (COV 1871) or call for informal interview

BATTERSEA COLLEGE OF TECHNOLOGY

(A COLLEGE OF ADVANCED TECHNOLOGY)
READER AND LECTURER IN METAL PHYSICS OR LOW TEMPERATURE PHYSICS

Applications are invited for the posts of Reader and Lecturer or Assistant Lecturer in the Physics Department. Preference will be given to candidates with interests in the physics of metals or of low temperatures, but appointments will not necessarily be restricted to this field. Appointment to the lectureship or assistant lectureship will be made according to qualifications and experience. Salary scales: Reader, £1,838 to £2,151; Lecturer, £1,408 to £1,601; Assistant Lecturer, £1,023 to £1,486 (including full allowances for good honours degree and training).

Further particulars may be obtained from the Clerk to the Governing Body, Battersea College of Technology, London, S.W.11.

NEW ZEALAND

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH

Applications are invited for the undermentioned vacancy:

Vacancy No. 549—Plant Breeder, Tobacco Research Station, Riwaka. The qualification desired for this position is an honours degree in science or agriculture. The Station is concerned with all aspects of the production of flue-cured tobacco and the successful applicant would be required to take an interest in all phases of the work. He would be primarily engaged in the breeding of improved varieties, with current emphasis on disease resistance. The salary offered as at April 1, 1961, is up to £1,700 a year depending on qualifications and experience. An outstanding officer can ultimately advance to £2,300 a year without administrative responsibility. Passages: Steamer fares of up to £165 each for the appointee and his wife, and pro rata for dependent children will be paid. Incidental expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and further details are available from the High Commissioner for New Zealand, 415 Strand, London, W.C.2, with whom applications will close on April 22, 1961. Please quote reference B.13/18/2 when inquiring.

LOUGHBOROUGH COLLEGE OF TECHNOLOGY

LEICESTERSHIRE
DEPARTMENT OF ELECTRICAL ENGINEERING

Applications are invited for a Research Fellowship for work on instrumentation and telemetering for physiological measurements on athletes. The Fellowship is tenable for up to three years at an annual value of £750 with contributory superannuation scheme. Some tutorial work or laboratory supervision may be undertaken, for which additional payment is made.

Application forms may be obtained from the Academic Registrar, quoting reference 20/AF/2.

BEECHAM GROUP

RESEARCH SCIENTIST

An opportunity with excellent prospects is being created by expansion activity in nutritional research.

A seasoned graduate (first- or second-class honours) is sought with experience in one or more of the following fields:

Biochemistry
Food Chemistry
Nutrition

A postgraduate qualification is desirable but appropriate experience would be an equivalent asset.

The successful applicant would work in the Basic Research Unit at Brentford and be directly responsible to the Manager of the Unit. Prospects are excellent for the right man.

Applications, giving full details of age, qualifications and experience, and quoting reference RS121, should be addressed to the Personnel Controller, Beecham Group Limited, Beecham House, Great West Road, Brentford, Middlesex.

GRADUATE CHEMIST AND SENIOR TECHNICIAN

A New Zealand company engaged in chemical industry has positions available for suitable persons who have either graduated in Chemistry or who have had experience as a technician in an industrial chemical laboratory. Selected applicants would receive assistance in emigrating to New Zealand and would be bound to serve with the company for a minimum period of two years.

Bona fide inquiries should be sent in the first instance by airmail to the Works Director, Ivon Watkins Limited, P.O. Box 144, New Plymouth, New Zealand. Following receipt of such inquiries, which should include as much information as possible giving age, marital status, qualifications and experience and accompanied by *copies only* of testimonials, arrangements will be made for interview in the United Kingdom (preferably in May) when the Managing Director will be visiting England. Inquirers will be advised of time and place of interview.

Ivon Watkins Limited is a New Zealand company actively engaged in the development of chemical industry and offers unique opportunities to graduates and technicians with some experience in chemical industry.

QUEENSLAND INSTITUTE OF MEDICAL RESEARCH

BRISBANE, AUSTRALIA

Applications are invited for the position of Director of the above Institute. The duties are (1) to direct research work and control research staff of the Institute, (2) to continue to develop the Institute on a comprehensive research basis, and (3) to plan the permanent housing of Institute. To date, research has been almost entirely in the field of communicable disease. The salary is £A.4,583 per annum. Tenure is for seven years, with eligibility for reappointment. Technical and lay staff, other than term appointees, such as the Director, are subject to the Public Service Acts, and administration generally follows Public Service practice. Appointee will be required to commence duty as early as possible after August 1, 1961.

Applications close, on April 30, 1961, with Agent-General for Queensland, 409 and 410 Strand, London, W.C.2, from whom intending applicants should obtain application forms and further information.

ISOTOPE APPLICATIONS UNIT, WANTAGE, Berks, of the National Chemical Laboratory, requires Scientific Officer to undertake chemical research using radioactive isotopes into problems of other D.S.I.R. and industrial Research Association Laboratories. Duties involve visits to laboratories in various parts of the country, ultimately in an advisory capacity. Qualifications: first- or second-class honours degree in chemistry or equivalent, preferably with few years postgraduate research experience. Salary scale £717 to £1,186 Prospects of promotion in mid-thirties to Principal Scientific Officer (£1,666 to £2,368).—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting ref. F.138/1A. Closing date April 8, 1961.

NOTTINGHAM NO. 2 HOSPITAL MANAGEMENT COMMITTEE

Applications are invited from persons holding an appropriate science degree, or the A.R.I.C., for the appointment of Senior Biochemist within the Nottingham No. 2 Group of Hospitals. The person appointed will work under the direction of the Chemical Pathologist at the City Hospital where there is a fully equipped biochemical laboratory. Salary scale £1,250 to £1,700 per annum.

Applications, stating age, experience and qualifications, with the names and addresses of two referees, should be sent to the undersigned as soon as possible.

J. H. HARGREAVES,
Group Secretary.
Sherwood Hospital, Nottingham.

THE METAL BOX COMPANY LIMITED

RESEARCH DEPARTMENT—
INFORMATION DIVISION

Applications are invited for the position of

INFORMATION ASSISTANT

in a team serving scientific and technical staff. Duties include the preparation of abstracts and summaries from the literature on packaging and food technology, and answering technical inquiries.

Previous experience in information work is not essential but applicants should have a broad technical background and must be capable of presenting information accurately in clear and concise English. Qualifications in science or technology at Advanced Level standard, or above, would be an advantage.

The position affords an opportunity to pursue a career in a growing profession of increasing importance and encouragement will be given to study for approved professional qualifications.

Starting salary in the range of £650 to £950 according to age, qualifications and experience.

Please apply in writing to:
Ref. A.W.,
Administration,
Research Department,
The Metal Box Company Limited,
Kendal Avenue, Westfields Road,
Acton, W.3.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

A post is available for a physiologist or zoologist, with interests and experience in the field of mammalian reproduction, in a small unit investigating the biochemical and physiological properties of cervical secretions, with particular reference to fertility. The work envisaged will involve a study, in co-operation with two biochemical colleagues, of the metabolism, motility and fertility of spermatozoa in cervical mucus and in fractions which can be separated from it. Good research facilities are available and the post offers an attractive opportunity for a scientist who wishes to work in a field bearing on this highly significant problem. The candidate will be expected to initiate and carry out work on the physiological side of the investigation.

Applicants should have a good degree in zoology or physiology, preferably with Ph.D. Appointment would be for three years in the first instance, salary in accordance with experience and qualifications. Applications to the Secretary, National Institute for Research in Dairying, Shinfield, Reading, Berks. Quote ref. 61/2.

MANSFIELD HOSPITAL MANAGEMENT COMMITTEE

Whole-time Biochemist (non-resident) required for hospital biochemical work in the Mansfield Area Pathology Service. The salary is that of the N.H.S. Basic Grade with a maximum of £1,035 per annum, the commencing salary being dependent upon qualifications and experience.

Applications to Hospital Secretary, King's Mill Hospital, Sutton-in-Ashfield, Notts.

PILKINGTON BROTHERS LIMITED

require an

ELECTRICAL ENGINEER

to take charge of the High Voltage Laboratory comprising power frequency and impulse test sections with test voltages of up to 1,500 kV. and 2,000 kV. respectively. An intensive programme of research and development relating to toughened glass power line insulators is in progress.

Applications, stating age, qualifications, experience and present salary should be addressed to the

Personnel Officer (Graduate Recruitment),
Pilkington Brothers Limited,
St. Helens, Lancashire.

UNIVERSITY OF SHEFFIELD

Applications are invited for the following positions in the Department of Fuel Technology and Chemical Engineering:

(1) a Research Fellowship, for work on the study of the Properties of Flames with the object of devising a method of detecting flames.

(2) a Research Fellowship or Bursary, according to experience, for work on the Aerodynamics of Flames and Boiler Combustion Chambers. The person appointed will be a member of a team investigating problems concerning the combustion of oil with special reference to applications to marine boilers.

The Department of Fuel Technology and Chemical Engineering has recently taken over newly built and equipped laboratories in which work is proceeding on a large number of combustion problems bridging the gap between fundamental knowledge and practical applications. Salary for either post according to age and experience. Candidates should have a good honours degree in mathematics, chemistry, physics, mechanical engineering, chemical engineering, or fuel technology.

Further particulars may be obtained from Professor M. W. Thring, the University, St. George's Square, Sheffield 1, to whom applications should be sent as soon as possible.

HILL FARMING RESEARCH ORGANIZATION

Applications are invited from graduates (male or female), or from those expecting to graduate in 1961, for a vacancy as Head of the Scientific Records Section at the Organization's headquarters in Edinburgh. Candidates should have studied mathematics or statistics as a principal subject in their university course. The appointment will be in either the Assistant Experimental Officer or the Experimental Officer grade, according to experience, the appropriate salary scales being as follows: Assistant Experimental Officer, £645 (age 22) to £983 per annum; Experimental Officer, £1,087 to £1,336 per annum.

Further particulars and application forms may be obtained from the Secretary of the Organization at 48 Palmerston Place, Edinburgh, 12. Closing date for applications is April 17, 1961.

UNIVERSITY COLLEGE OF SWANSEA

Applications are invited from suitably qualified candidates for an Assistant Lectureship or Lectureship in Pure Mathematics. Salary scales: Lectureships, £1,050 to £1,850 per annum; Assistant Lectureships, £800 to £950 per annum. F.S.S.U. benefits and family allowances.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies) must be received not later than Saturday, April 29, 1961.

THE LONDON HOSPITAL, WHITECHAPEL, E.1, has vacancy in their Physics Department for a Physicist in the Basic Grade. Applicants should have an honours degree in physics but previous experience of hospital physics is not essential. The work is chiefly on radiation physics applied to radiotherapy but there will be opportunities to gain experience in the applications of radioisotopes in medicine and also to participate in development and research. Salary £670 to £1,200.—Applications with the names of two referees to the House Governor.

PROGRESSIVE PHARMACEUTICAL COMPANY

in South Cheshire requires a Chemist (Hon.B.Sc. or A.R.I.C.) to work on own initiative under supervision of a research manager. The duties would require the applicant to interest himself in a wide range of problems connected with the development and control of pharmaceuticals including biological materials.

Experience of modern analytical techniques would be an advantage. The post is permanent, pensionable, and offers real interest and excellent prospects to the right man who should be 25 to 30 years of age.

Applications, which should be submitted in full, will be treated in the strictest confidence. Write to Box No. 959, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

U.S.A.
UNIVERSITY OF ALABAMA MEDICAL SCHOOL

GENERAL BIOCHEMIST

Biochemist required for Gastroenterology Research Laboratories with special interest in gastric secretion (electrolytes, pepsin), small bowel absorption and lipid analysis. Research experience essential. Starting salary according to experience, but would not be less than $7,000 per annum.

MEDICAL TECHNICIAN

Medical Technician required for Gastroenterology Research Laboratories with special interest in gastric secretion (electrolytes, pepsin), small bowel absorption and lipid analysis. Research experience desirable but not essential.

Applications should be addressed to:
Basil I. Hirschowitz, M.D.,
Director, Division of Gastroenterology,
University of Alabama Medical Center,
Birmingham, Alabama.

NORTH OF SCOTLAND COLLEGE OF AGRICULTURE

Applications are invited for the post of Assistant Advisory Officer in the Bacteriology Department. Applicants should have a degree in science preferably with honours or equivalent. Graduates in agriculture or dairying with bacteriology and students graduating at the end of the present session will also be considered. Appointment will be to one of the following salary scales: Grade III, £1,004 to £1,570 per annum (National); Grade IVa, £738 to £993 per annum (National); Grade IVb, £718 to £993 per annum (National). The person appointed will be required to take up duty in July/August next and will assist with the Advisory and Investigational work of the Department. Some lecturing to Diploma students may also be required. Superannuation scheme. Medical examination.

Forms of application may be obtained from the Secretary of the College, 41½ Union Street, Aberdeen, with whom applications should be lodged not later than April 29, 1961.

UNIVERSITY OF SYDNEY
LECTURESHIP IN HISTOLOGY AND EMBRYOLOGY

Applications are invited for the above-mentioned position. The salary for a Lecturer is within the range £A.1,730 by £A.105 to £A.2,435 per annum, plus cost of living adjustments (at present £A.36 per annum) and will be subject to deductions under the State Superannuation Act. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. Under the Staff Members' Housing Scheme in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 5, 1961.

MOREDUN INSTITUTE
EDINBURGH

Research worker in virus diseases. Experience with tissue culture techniques an advantage. Appointment Scientific Officer, Senior Scientific Officer or Principal Scientific Officer, according to qualifications, age and experience.

Apply in writing to the Secretary, Animal Diseases Research Association, Moredun Institute, Gilmerton, Edinburgh, 9.

MIDDLESEX HOSPITAL MEDICAL SCHOOL
DEPARTMENT OF BIOLOGY AS APPLIED TO MEDICINE

Applications are invited for the post of Assistant Lecturer in the Department, the appointment to begin in October, 1961. The successful candidate will be expected to participate in the teaching of pre-medical, medical and postgraduate students, but ample opportunities will be offered for research. Preference will be given to candidates with research experience in some field of experimental zoology.

Applications, in triplicate and with the names of two referees, should be made before July 1, 1961, to the Secretary, Department of Biology as Applied to Medicine, Middlesex Hospital Medical School, London, W.1, from whom further particulars can be obtained.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY
(FACULTY OF TECHNOLOGY IN THE UNIVERSITY OF MANCHESTER)

Appointment of
LECTURER IN CIVIL ENGINEERING

Applications are invited for a Lectureship in Civil Engineering, with the title and status of Lecturer in the University of Manchester. Good research facilities are available in Hydraulics, Soil Mechanics, Highway Engineering, and Public Health Engineering: applicants should have a special interest in one of these branches or an allied subject. (Structural Engineering is covered in a separate department.) Salary, according to qualifications and experience, in the scale £1,050 to £1,850 per annum. Superannuation under the F.S.S.U. Family allowances.

Conditions of appointment and form of application may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1. The last day for the receipt of applications is Saturday, April 29, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for a Senior Lectureship in Electrical Engineering, in the Department of Electrical Engineering, Queen's College, Dundee, to commence not later than October 1, 1961. Candidates should possess at least a good honours degree in electrical engineering or physics and suitable experience in teaching and/or research, preferably with a special interest in electronics. Salary scale: £1,925 by £75 to £2,425. F.S.S.U. family allowance. Grant towards furniture removal expenses.

Applications (six copies), containing the names of three referees, to the undernoted, from whom further particulars may be obtained, not later than April 22, 1961.

PATRICK CUMMING,
Joint Clerk to the University Court.
Queen's College, Dundee.

THE DISTILLERS COMPANY LIMITED

RUBBER TECHNOLOGIST

The Company has a vacancy for a Rubber Technologist at the Barry, Glamorgan, factory of the Plastics Division.

The duties at Barry involve technical service work, particularly the improvement of the properties of rubber compositions by the addition of synthetic resins. The man appointed will have one or more assistants as required.

Candidates, aged not over 35, must have at least four years' practical experience in the rubber industry. They should hold a qualification of the Institution of the Rubber Industry, or its equivalent, and provided they have the required technological experience, candidates holding H.N.C. in Chemistry will be considered.

Write:
STAFF MANAGER,
THE DISTILLERS COMPANY LIMITED
21/22 BOLTON STREET
LONDON, W.1.

Quote Ref. 15/61.N

DIRECTOR OF THE ROYAL SCOTTISH MUSEUM
EDINBURGH

Applications are invited for this pensionable post (salary £3,350) which will be vacant on October 1, 1961. The Museum comprises Departments of Art and Ethnography, Natural History, Technology, and Geology, and contains galleries for permanent and temporary exhibitions, a new lecture theatre, and a reference library.

Candidates (men or women) must be at least 40 on May 1, 1961. They must have had suitable experience of museum administration and practice and should preferably have achieved distinction in one of the fields of study with which the Museum is concerned.

Write Secretary (Establishment), Scottish Education Department, St. Andrew's House, Edinburgh, 1, for application form and further particulars. Closing date April 17, 1961.

UNIVERSITY OF CAMBRIDGE

Applications are invited for a University Demonstratorship in Botany, with especial reference to Cytology and Genetics, from October 1, 1961. Pensionable stipend in scale £900 by £50 to £1,150, plus children's allowances.

Further particulars from Dr. C. B. Goodhart, Museum of Zoology, Downing Street, Cambridge, to whom applications must be sent by April 17, 1961.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Applications are invited for a Lectureship in Mineral Technology. Salary in range £1,050 to £1,850 per annum, according to qualifications, plus £60 per annum London allowance, family allowances and F.S.S.U. membership. The successful candidate will be required to organize and take charge of a course on the chemical and engineering principles of liquid-solid and gas-solid processes for the treatment of ores and minerals, including leaching, drying and roasting. He should also be qualified to conduct and supervise research in this field.

Applications, with full details of qualifications and experience, to Dr. M. G. Fleming, Imperial College of Science and Technology, London, S.W.7.

UNIVERSITY COLLEGE
ADDIS ABABA
ETHIOPIA

Lecturers in Accounting, English Language and Literature, Geography, Pharmacy, Biochemistry, Inorganic Chemistry, Botany, Mathematics, Physics, Statistics, Zoology (Comparative Anatomy). Annual net salary £1,741 to £2,500 according to qualifications and teaching experience. Accommodation and passage.

Apply to President, University College, P.O.B. 199, Addis Ababa, Ethiopia.

UNIVERSITY OF CAMBRIDGE
SCHOOL OF AGRICULTURE

Applications are invited for the post of research biochemist to join a team investigating the effects of heat treatment on nutritional availability of the amino acids in the proteins of foods. Qualifications should include postgraduate research experience in the fields of protein chemistry or nutrition. The post is tenable for a maximum period of five years. Salary equivalent to University scales and in accordance with age, qualifications and experience.

Applications, giving full details of the candidate's qualifications and experience, together with the names and addresses of three referees, should be sent to the Secretary, School of Agriculture, Downing Street, Cambridge, to reach him not later than April 7, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for the post of Research Assistant in the Wellcome Laboratories of Pharmacology, the Gatty Marine Laboratory, St. Andrews. Candidates should be suitably qualified in biochemistry, pharmacology or zoology for work on thyroid metabolism of lower vertebrates. Suitable candidates may register for a higher degree. Salary scale £700 to £800; appointment for three years in the first instance.

Applications, with names of three referees, should be lodged, not later than March 31, 1961, with the Joint Clerk to the University Court, College Gate, St. Andrews.

UNIVERSITY OF EDINBURGH
DEPARTMENT OF ZOOLOGY

Applications are invited for the post of Assistant in the Department of Zoology. Salary scale: £800 by £50 to £950 per annum, with superannuation benefit and family allowance where applicable. Tenure is normally for three years, with two possible annual extensions. The Assistant will be required to help in the general teaching of the Department, and will have ample facilities for research.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees, should be lodged as soon as possible, and not later than April 15, 1961.

CHARLES H. STEWART,
Secretary to the University.

CITY GENERAL HOSPITAL
SHEFFIELD, 5

Applications are invited immediately for the post of Senior Technician (Grade 1) or Scientific Officer for Microbiological Assay Unit (Vitamin B12 and folic acid). Salary on scale according to grading, i.e., Senior Technician 1, £710 to £780; Scientific Officer, £730 to £925 (candidates possessing first- or second-class honours degree or Associate or Graduate Membership of the Royal Institute of Chemistry), or £650 to £925 (candidates possessing other appropriate science degrees). Whitley Council conditions of service.

Apply, giving full details of age, experience, etc., and the names of two referees, to the Group Secretary, Sheffield No. 1 Hospital Management Committee "Lyndhurst," Nether Edge Hospital, Sheffield, 11.

PHYSICAL CHEMISTS

A research programme of great scope and interest covers high polymers, inorganic and organic pigments, etc., in surface coatings over a variety of substrates. Physical chemists are required for basic work in this field. Previous research experience although desirable is not essential. Salaries will be commensurate with age and experience, with F.S.S.U. superannuation.

Applications, giving full details of qualifications and experience, and the names of two referees, should be made, in writing, to the Director, the Research Association of British Paint, Colour and Varnish Manufacturers, Paint Research Station, Waldegrave Road, Teddington, Middlesex.

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Post-doctoral Fellowship available for a biochemist or an organic chemist with biological interests. The Fellow will work with K. S. Dodgson on the chemistry and biochemistry of hydroxylated amino acids and related compounds. Appointment will be for one year in the first instance with a possibility of renewal for a further two years. Salary up to £1,000 per annum.

Applications to be sent before April 21 to the Professor of Biochemistry, University College, Newport Road, Cardiff.

ONTARIO VETERINARY COLLEGE
GUELPH, ONTARIO, CANADA

Applications are invited for an appointment as an Assistant or Associate Professor in Pharmacology. Applicants should have a Ph.D. and teaching experience. The candidate will lecture to undergraduate and postgraduate students in pharmacology and be expected to undertake research in some aspect of the field.

A curriculum vitae and references should be addressed to Dr. H. G. Downie, Professor and Head, Department of Physiological Sciences.

ESSEX COLLEGE
ASSUMPTION UNIVERSITY OF WINDSOR WINDSOR, ONTARIO, CANADA

The Department of Physics invites applications for the following appointments: two Experimental Physicists, one Theoretical Physicist. The successful applicants will be expected to instruct undergraduate and graduate students and devote a part of their time to research. Preference will be given to candidates with interests in low energy nuclear physics, solid state physics, or molecular spectroscopy. The rank and salary will depend upon qualifications and experience, but the salary will not be less than $7,000 at Ph.D. level.

Inquiries should be addressed to the Chairman, Department of Physics, Assumption University of Windsor.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer for work at the University Tidal Institute and Observatory. Preference will be given to candidates with an honours degree in mathematics. The initial salary will be within the range £800 to £1,250 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than April 4, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting reference CV/N.

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Applications are invited for the post of Lecturer or Assistant Lecturer, in accordance with age and qualifications, in the Department of Physics from October 1, 1961.

Further particulars may be obtained from the Registrar to whom six copies of applications (containing the names of three referees), should be sent not later than April 21, 1961.

E. R. EVANS,
Registrar.

Cathays Park,
Cardiff.

QUEEN MARY COLLEGE
(UNIVERSITY OF LONDON)

Applications are invited for appointment as Research Fellow in Plant Biochemistry in the Department of Botany, whose duties will be to participate in research on the mechanism of photosynthesis. Applicants should have a first degree in biochemistry, chemistry or botany and research experience in biochemistry and particularly in the use of radioactive tracers. The appointment is for one year in the first instance. Initial salary, within the range £900 to £1,100 according to qualifications and experience.

Application forms, obtainable from the Registrar, Queen Mary College, Mile End Road, London, E.1, to be returned by April 7.

OLDCHURCH HOSPITAL ROMFORD, ESSEX
(709 Beds)
RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Moulc Room work. Instrument or Physics Workshor experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

ROYAL BOTANIC GARDENS, KEW: Assistant Curator. Pensionable post for man or woman at least 25 on March 1, 1961, with sound general education and practical and theoretical knowledge of horticulture. N.D.H. or university degree in appropriate subjects an advantage. Preference given to those trained in Botanic Gardens or similar Institutions who have had experience in supervision of staff. Starting salary £804 (£877 with N.D.H. or equivalent) at 25 to £914 (£986 with N.D.H. or equivalent) at 28 or over, rising to £1,386; salary scales under review. House provided.—Write, Civil Service Commission, Burlington Gardens, London, W.1, for application form, quoting 5287/61. Closing date, April 13, 1961.

CHARING CROSS GROUP OF HOSPITALS has vacancy for a Physicist (Principal Grade) in Radiotherapy Department. Salary on the scale £1,750 to £2,125 plus London weighting.—Write, giving two names and addresses for reference, to House Governor (A), Charing Cross Hospital, W.C.2. Closing date April 5.

VETERINARY OFFICERS, RESEARCH Officers, Assistant Veterinary Investigation Officers: Ministry of Agriculture, Fisheries and Food. Pensionable posts for men and women aged at least 23. M.R.C.V.S. normally required, and postgraduate experience desirable. Present vacancies for Research Officers in virology, bacteriology, and biochemistry. National salary scales £926 (at 23) to £1,269 (at 32 or over) rising to £1,420, then to £1,778. Promotion prospects.—Write Civil Service Commission, Burlington Gardens, London, W.1, for application form, quoting 130-173-265/61. Early application advised.

ESSEX COLLEGE
ASSUMPTION UNIVERSITY OF WINDSOR WINDSOR, ONTARIO, CANADA

The Department of Physics offers Graduate Assistantships to candidates wishing to proceed to an M.Sc. in physics. Stipend up to $2,000 for eight months, depending on qualifications and duties in the department. There is a possibility of additional income during the summer months. At present research is proceeding in beta-ray spectroscopy, optical pumping, molecular collision problems, and electromagnetic interactions in shock waves.

Inquiries should be addressed to the Chairman, Department of Physics, Assumption University of Windsor.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

CHEMISTRY DEPARTMENT, UNIVERSITY of Southampton. Applications are invited for the Union Carbide Postdoctoral Fellowship in Organic Chemistry. Salary £850 to £1,000 per annum tenable for up to three years.—Applications, giving details of qualifications and names of two referees, should be sent to Professor R. C. Cookson, The University, Southampton.

TECHNICIAN (FEMALE) REQUIRED FOR new expanding Physics Laboratory. Salary at minimum age 21: £570 rising to £710 per annum. Qualifications G.C.E. "A" level in physics and mathematics or similar. Work chiefly concerned with diagnosis and treatment using radioactive isotopes. Alternatively, Technician-in-Training. Salary at age 16, £215 rising to £440 per annum, with prospects of promotion to Technician on obtaining requisite qualifications.—Further particulars from Hospital Secretary, Dudley Road, Hospital, Birmingham 18.

RESEARCH CHEMIST WANTED BY FIRM producing alloys and compounds of the "rarer" metals. The work will include investigation of treatment on both laboratory and pilot plant scale. An interest in new analytical methods would be an advantage (spectrographic, spectrophotometric and chromatographic methods are in routine use in the laboratory). Applicants should have at least a second-class honours degree or equivalent, but initiative and originality are more important than previous research experience. Starting salary approximately £1,000 per annum. Three weeks' annual holiday. A pension scheme is in operation.—Apply to London and Scandinavian Metallurgical Co. Ltd., Fullerton Road, Rotherham, Yorkshire.

ASSISTANT TO THE CHIEF ENGINEER

Painton & Co. Ltd., manufacturers of high quality components for the Electronics Industry, are expanding their activities and wish to appoint an Assistant to the Chief Engineer. Applicants must be graduates in physics or electrical engineering, have experience in the design and development of electronic components and be able to carry executive authority. This is a staff appointment with superannuation scheme.

Applications to the Personnel Officer, Kingsthorpe, Northampton.

SENIOR TECHNICIAN REQUIRED FOR biochemistry laboratory, Department of Pathology, Welsh National School of Medicine. I.M.L.T. qualification or science degree desirable. The work involves routine analyses, especially in connexion with the "Artificial Kidney." Salary in accordance with National Health Service scale.—Applications, quoting two referees, to Steward and Finance Officer, Pathology Department, Royal Infirmary, Cardiff.

BIOCHEMIST. A MALE GRADUATE WITH some years experience is required by the Research Laboratories of the British Drug Houses Ltd. The work is concerned mainly with the identification and assay of drug metabolites and with aspects of protein chemistry. The company offers good conditions, including a Superannuation Fund with Life Assurance and Profit Sharing Scheme.

Applications, with full details, to Personnel Manager, Ref. HAC/VP, the British Drug Houses Ltd., Graham Street, N.1.

PLASTICS TECHNOLOGIST

A Plastics Technologist is required for the Technical Department of an expanding Company in the West of Scotland. He will be concerned with the development of manufacturing techniques and the pilot plant production of a new plastic component. A degree, or its equivalent, is the preferred qualification, and experience of processing plastics, preferably thermoplastics, is essential. Experience in precision injection moulding, compounding and in mould design would be an advantage. The position affords considerable opportunity for original and interesting work in a field which is a departure from the Company's established range of products.

A starting salary up to £1,200 per annum is offered.

Applications containing brief details of relevant data should be sent to Box 958, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Technician at the Marine Biological Station, Port Erin, Isle of Man. Basic salary in the range £490 to £675 per annum. Supplementary payments to basic salary will be made for the possession of appropriate qualifications.

Applications, giving the names of two referees, and quoting reference number 260, should be made in writing to the Registrar, the University, Liverpool, 3, before April 4, 1961. Quoting reference CV/N.

ASSISTANT PROFESSOR OF PHYSIOLOGY

THE UNIVERSITY OF ALBERTA

invites applications for the position of Assistant Professor of Physiology effective not later than September 1, 1961, at a minimum salary of $6,500 per annum with annual increments. Duties include undergraduate and graduate teaching and a programme of research. This Department is seeking a Cellular Physiologist, and some preference will be given to candidates with experience in electron microscopy.

Inquiries for further information are welcomed by the Head of the Department of Physiology. Applications should include transcripts of records, a recent photograph, curriculum vitae, and the names of three referees, and should be addressed to the Dean of Medicine, University of Alberta, Edmonton, Alberta, Canada.

BEDFORD COLLEGE

(UNIVERSITY OF LONDON)
REGENT'S PARK, LONDON, N.W.1

The Council invites applications from honours graduates for two Assistant Lectureships (i) in Physiology, and (ii) in Biochemistry. Vacant October 1, 1961; open to men and women. Salary scale £800 by £50 to £950, plus £60 per annum London allowance, initial salary according to qualifications and experience. Closing date for applications April 28, 1961.

Full particulars from the Secretary.

THE POLYTECHNIC

309 REGENT STREET, LONDON, W.1
DEPARTMENT OF CHEMISTRY AND BIOLOGY
POSTGRADUATE RESEARCH IN ORGANIC CHEMISTRY

A limited number of vacancies exist for Research Students during the session beginning September 25, 1961. Facilities exist for successful candidates to study for higher degrees and to undertake part-time teaching of chemistry.

Applications should be made, as soon as possible, to the Head of the Department of Chemistry and Biology.

ROWETT RESEARCH INSTITUTE

Applications are invited for a research appointment in the Pig Section of the Applied Nutrition Department. The post is superannuated and will be in the Scientific Officer or Senior Scientific Officer grade according to experience. Applicants should have previous experience in research although not necessarily with pigs. Salary scales (Provincial): Scientific Officer, £717 to £1,186 per annum; Senior Scientific Officer, £1,302 to £1,604 per annum.

Applications, stating date of birth with particulars of education and experience, and the names of three referees, should be sent to the Secretary, Rowett Research Institute, Bucksburn, Aberdeen.

UNITED NEWCASTLE UPON TYNE HOSPITALS

ROYAL VICTORIA INFIRMARY

Applications are invited for a post of Medical Laboratory Technician in the Department of Dermatology at the Royal Victoria Infirmary, Newcastle, to assist in research on skin physiology, cell metabolism and serum protein disturbances in immunological reactions. Salary and conditions of service will be those agreed by the Whitley Councils for the Health Services.

Applications, giving two referees, should be sent to the House Governor and Secretary, Royal Victoria Infirmary, Newcastle.

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS

Agricultural Graduate to assist with farm management. Aptitude for field experimentation essential. Starting salary according to age and experience in range £578 to £983, or £1,057 to £1,336. Superannuation scheme. House to rent.

Apply to Secretary, giving full details of training and practical experience and names of two referees.

DAIRY RESEARCH INSTITUTE

NEW ZEALAND

Applications are invited for the following research staff. Chemist for research on the chemistry of dairy products. Biochemist-Bacteriologist for work mainly in connection with the manufacture and ripening of cheese. Salaries are in the ranges £900 to £1,210, £1,250 to £1,700, £1,750 to £2,000. Travel and other removal expenses are allowed within certain limits.

Further particulars may be obtained in Britain from Mr. P. S. Robertson, c/o N.I.R.D., Shinfield, near Reading.

APPLICATIONS INVITED FOR POST OF Senior Technician (male) in the Biology Department of Repton School, Repton, Derby. Salary £450 to £720, position on scale dependent upon experience.—Write with testimonial and name of referee to Mr. W. A. C. Bullock, Senior Biologist, Repton School, giving full details of qualifications and experience.

A VACANCY EXISTS FOR A RESEARCH Assistant in the Radioisotope Unit Postgraduate Medical School, to work on applications of radioisotopes in clinical medicine and research. Candidates should have a first- or second-class honours degree in the physical or biological sciences. The successful candidate will be encouraged to undertake studies leading to a higher degree. Salary according to experience on a scale £750 by £50 to £950.—Applications, together with the names of two referees, should be forwarded by April 15, to: Secretary, Postgraduate Medical School, Ducane Road, W.12.

NUCLEAR CHEMISTRY GRADUATE APpointments open beginning July or September, 1961, at stipends from $1,920 to $2,520 for fundamental work toward M.S. or Ph.D. degree. Twelve-month appointment with one month vacation. Excellent equipment for research on neutron induced nuclear reactions and decay schemes of radioactive nuclei using 400 KV. Cockcroft-Walton ion accelerator.—Write: Department of Chemistry, University of Arkansas, Fayetteville, Ark., U.S.A.

E.M.I.

ASSISTANT ANALYTICAL CHEMIST

The Emitape Division of E.M.I. Ltd. have a vacancy for a young chemist, male or female, to do general analysis in connection with surface coatings, resins, solvents and plastics.

Applicants should have previous industrial experience and have qualifications up to H.N.C. standard. A contributory pension scheme is in operation and there are full sports, canteen and welfare facilities.

Please write, quoting reference SS/R/L3, to:

Personnel Manager,
E.M.I. Limited,
Blyth Road,
Hayes, Middlesex.

A TECHNICIAN IS REQUIRED WHO possesses the Final I.M.L.T. in biochemistry or an equivalent examination. Duties will consist of biochemical research under the personal charge of the Professor.—Apply in writing to the Secretary, Institute of Neurology, the National Hospital, Queen Square, London, W.C.1, not later than April 8, 1961.

MISCELLANEOUS

SCIENTISTS-TRANSLATORS

Russian to English

Supplement your income while you keep abreast of latest Soviet research in your field. GUARANTEED steady flow of translation *in your specialty*. Must have graduate study and experience in one of the following disciplines:

Chemistry (organic, inorganic, physical, structural). Physics (atomic, plasma, solid state). Crystallography. Instrumentation, Automation. Biology (microbiology, bacteriology, epidemiology). Botany. Native command of English necessary.

Chinese-English scientist-translators also wanted.

Consultants Bureau, 227 W.17 Street, N.Y. 11, N.Y.

MURDOCH TRUST

For the BENEFIT of INDIGENT BACHELORS and WIDOWERS of good character, over 55 years of age, who have done "something" in the way of promoting or helping some branch of Science.

Donations or pensions may be granted to persons who comply with these conditions.

For particulars, apply to MESSRS. SHEPHERD & WEDDERBURN, W.S., 16 Charlotte Square, Edinburgh, 2.

STAFFORDSHIRE COUNTY COUNCIL EDUCATION COMMITTEE

STAFFORD COLLEGE OF TECHNOLOGY

Tenders are invited for (a) Demonstration electrical equipment for electrical laboratories. (b) Major items of apparatus for chemical laboratory. (c) X-ray apparatus for nucleonic block.

Forms of Tender may be obtained from the Director of Education (Supplies), County Education Offices, Earl Street, Stafford.

Completed Tenders enclosed in the envelope provided must be received by the undersigned at County Buildings, Martin Street, Stafford, not later than Noon, Saturday, April 29, 1961.

T. H. EVANS,
Clerk of the County Council.

TRADE ANNOUNCEMENTS

BRIGHT'S REMOTE COLD CONTROLLED Microtome (cryostat) custom built for producing frozen sections for rapid diagnostic biopsies.—Full information on request to Bright's Refrigerator Service Ltd., 399 Portobello Road, London, W.10. LADbroke 4153.

LECTURES AND COURSES

UNIVERSITY OF SHEFFIELD
Residential Course on

SOLID FUEL COMBUSTION

Fundamental Studies and their applications in Practical Problems
Director of Studies: Professor M. W. Thring, M.A., F.Inst.F., F.Inst.P., M.I.Chem.E., Professor of Fuel Technology and Chemical Engineering, University of Sheffield
July 9 to 15, 1961
Further information may be obtained from the Director of Extramural Studies, St. John's, Crookes Valley Road, Sheffield 10. (Telephone: 65212).

CUMBERLAND EDUCATION COMMITTEE

WHITEHAVEN COLLEGE OF FURTHER EDUCATION

Flatt Walks, Whitehaven. Telephone 2976

PRINCIPAL: J. Nicholson, B.Sc., A.R.I.C., A.I.M., F.C.S., F.R.S.A., Dip. Ed.

DEPARTMENT OF CHEMISTRY

ONE-DAY SYMPOSIUM

ON

"RECENT DEVELOPMENTS IN THE ANALYSIS OF METALS"

Thursday, May 4, 1961

MORNING

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Applications are invited for the above course from Honours graduates in either Chemistry, Biochemistry, Botany, Zoology or Genetics. The course, which is of one year duration, will involve short lecture courses, training in research techniques, and research under the direction of a supervisor. The course can lead to the degree of M.Sc. by thesis. The D.S.I.R. have accepted the course as suitable for the ward of Advanced Course Studentships.

All applications, giving details of career, degree course, etc., should be sent to Professor S. R. Elsden, Department of Microbiology, The University, Sheffield, 10.

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SESSION 1961-62

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FOR SALE. *GMELIN. HANDBUCH DER anorganischen Chemie*. 8th edn. Complete to December, 1959, except for supplementary vols. to No. 13 and 33; vol. 15B; and part 59F.II.2. Price £1,650, delivered U.K. Present cost over £2,100.—Box 960, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

WANTED: WEYON—*PROTOZOOLOGY*. 2 vols., 1926.—Burton-Garbett, 8 Merton Rise, London, N.W.3.

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Application forms and further particulars may be obtained from the University or from the Secretary, the Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications should reach the University by April 30 or October 31 in any year, although special consideration may be given to applications at other times. Scholarships may be taken up at any time after award, subject to agreement of the Head of Department concerned.

D. K. R. HODGKIN,
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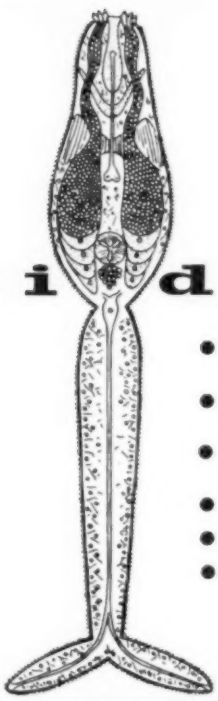

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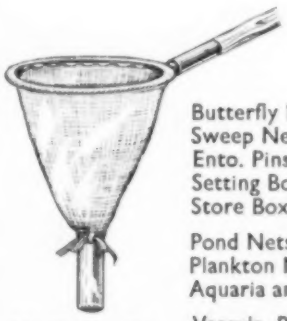

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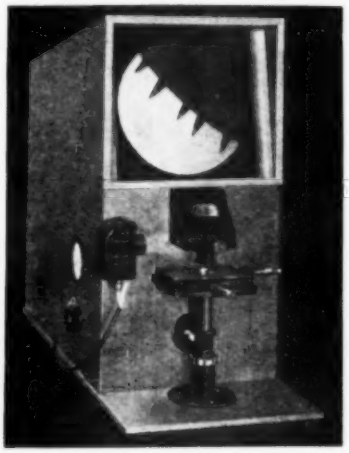

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surface activity

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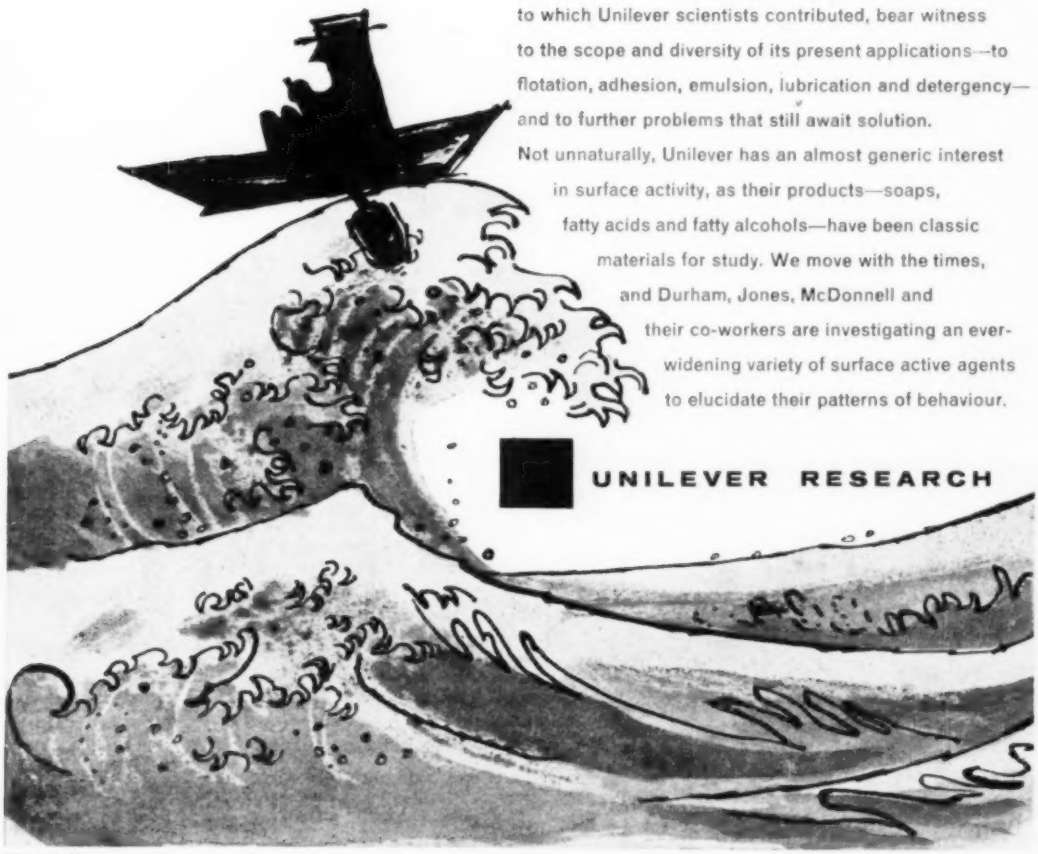

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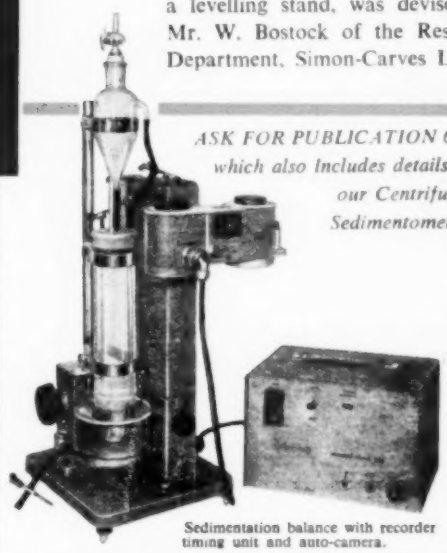

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